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Early Intensive Behavioral Intervention (EIBI) for Young Children with Autism Spectrum Disorders (ASD): A Systematic Review

Brian Reichow, Erin E Barton, Brian A Boyd, Kara Hume



Colophon

Title Early Intensive Behavioral Intervention (EIBI) for Young Children with

Autism Spectrum Disorders (ASD): A Systematic Review

Authors Brian Reichow¹

Erin E Barton² Brian A Boyd³ Kara Hume⁴

¹Child Study Center, Yale University School of Medicine, USA.

²School of Education and Human Development,

University of Colorado Denver, USA

³Division of Occupational Science and Occupational Therapy, Department of Allied Health Sciences, University of North Carolina at Chapel Hill, USA. ⁴Frank Porter Graham Child Development Institute, University of North

Carolina at Chapel Hill, USA

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Corresponding Brian Reichow, author Child Study Center,

Yale University School of Medicine,

230 South Frontage Road, POBOX 207900,

New Haven, CT, 06520-7900, USA.

brian. reichow @yale.edu.

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The Campbell Collaboration P.O. Box 7004 St. Olavs plass

0130 Oslo, Norway

www.campbellcollaboration.org

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Plain Language Summary

Early intensive behavioral intervention (EIBI) for increasing functional behaviors and skills in young children with autism spectrum disorders (ASD).

Early intensive behavioral intervention (EIBI) is one of the most widely used treatments for children with autism spectrum disorder (ASD). The purpose of our review was to examine the research on EIBI. We found a total of five studies that compared EIBI to generic special education services for children with ASD in schools. Only one study randomly assigned children to a treatment or comparison group, which is considered the 'gold standard' for research. The other four studies used parent preference to assign children to groups. We examined and compared the results of all five studies. A total of 203 children (all were younger than six years old when they started treatment) were included in the five studies. We found that children receiving the EIBI treatment performed better than children in the comparison groups after about two years of treatment on tests of adaptive behavior (behaviors that increase independence and the ability to adapt to one's environment), intelligence, social skills, communication and language, autism symptoms, and quality of life. The evidence supports the use of EIBI for some children with ASD. However, the quality of this evidence is low as only a small number of children were involved in the studies and only one study randomly assigned children to groups.

Abstract

BACKGROUND

The rising prevalence of autism spectrum disorders (ASD) increases the need for evidence-based behavioral treatments to lessen the impact of symptoms on children's functioning. At present, there are no curative or psychopharmacological therapies to effectively treat all symptoms of the disorder. Early intensive behavioral intervention (EIBI), a treatment based on the principles of applied behavior analysis delivered for multiple years at an intensity of 20 to 40 hours per week, is one of the more well-established treatments for ASD.

OBJECTIVES

To systematically review the evidence for the effectiveness of EIBI in increasing the functional behaviors and skills of young children with ASD.

SEARCH METHODS

We searched the following databases on 22 November 2011: CENTRAL (2011 Issue 4), MEDLINE (1948 to November Week 2, 2011), EMBASE (1980 to Week 46, 2011), PsycINFO (1806 to November Week 3, 2011), CINAHL (1937 to current), ERIC (1966 to current), Sociological Abstracts (1952 to current), Social Science Citation Index (1970 to current), WorldCat, metaRegister of Controlled Trials, and Networked Digital Library of Theses and Dissertations. We also searched the reference lists of published papers.

SELECTION CRITERIA

Randomized control trials (RCTs), quasi-randomized control trials, or clinical control trials (CCTs) in which EIBI was compared to a no-treatment or treatment-as-usual control condition. Participants must have been less than six years of age at treatment onset and assigned to their study condition prior to commencing treatment.

DATA COLLECTION AND ANALYSIS

Two authors independently selected and appraised studies for inclusion and assessed the risk of bias in each included study. All outcome data were continuous, from which standardized mean difference effect sizes with small sample correction were calculated. We conducted random-effects meta-analysis where possible, which means we assumed individual studies would provide different estimates of treatment effects.

MAIN RESULTS

One RCT and four CCTs with a total of 203 participants were included. Reliance on synthesis from four CCTs limits the evidential base and this should be borne in mind when interpreting the results. All studies used a treatment-as-usual comparison group. We synthesized the results of the four CCTs using a random-effects model of meta-analysis of the standardized mean differences. Positive effects in favor of the EIBI treatment group were found for all outcomes. The mean effect size for adaptive behavior was g = 0.69 (95% CI 0.38 to 1.01; P < 0.0001). The mean effect size for IQ was g = 0.76 (95% CI 0.40 to 1.11; P < 0.0001). Three measures of communication and language skills all showed results in favor of EIBI: expressive language g = 0.50 $(95\% \ CI \ 0.05 \ to \ 0.95; \ P=0.03)$, receptive language $g=0.57 \ (95\% \ CI \ 0.20 \ to \ 0.94; \ P=0.03)$ = .03), and daily communication skills g = 0.74 (95% CI 0.30 to 1.18; P = 0.0009). The mean effect size for socialization was g = 0.42 (95% CI 0.11 to 0.73; P =0.0008), and for daily living skills was g = 0.55 (95% CI 0.24 to 0.87; P = 0.0005). Additional descriptive analyses of other aspects related to quality of life and psychopathology are presented. However, due to the inclusion of non-randomized studies, there is a high risk of bias and the overall quality of evidence was rated as 'low' using the GRADE system, which rates the quality of evidence from metaanalyses to determine recommendations for practice.

AUTHORS' CONCLUSIONS

There is some evidence that EIBI is an effective behavioral treatment for some children with ASD. However, the current state of the evidence is limited because of the reliance on data from non-randomized studies (CCTs) due to the lack of RCTs. Additional studies using RCT research designs are needed to make stronger conclusions about the effects of EIBI for children with ASD.

1 Background

1.1 DESCRIPTION OF THE CONDITION

The pervasive developmental disorders (that is, Autistic Disorder, Asperger's Disorder, Pervasive Developmental Disorder - not otherwise specified, Atypical Autism, Rett's Disorder, and Childhood Disintegrative Disorder, as defined by the Diagnostic and Statistical Manual for Mental Disorders (DSM IV, though likely modified by the DSM V due in 2013) are early-onset conditions characterized by delay and deviance in the development of social, communicative, and other skills (WHO 1994; APA 2000). The term 'autism spectrum disorders' (ASD) is the common clinical nomenclature used to define these lifelong disorders that impact the brain and behavior of affected individuals (Baird 2006). Individuals with ASD are diverse in their symptom presentation; for example, some individuals avoid social contact while others are overly social and intrusive. They also vary greatly in cognitive functioning level (for example, from severe intellectual disability to well above average intelligence) and their ability to function in real life situations (for example, from living in an institutional setting to full independent living with a spouse and children). International prevalence estimates of ASD suggest it affects 1% of children in the population (Baird 2006; Kuehn 2007), making it more prevalent than childhood cancer or juvenile diabetes. Prevalence studies have consistently indicated more boys are diagnosed with ASD than girls; the reported ratio is approximately four boys for every girl (Fombonne 2005). A lifelong condition such as this often has long-term societal and familial costs associated with it. In the USA, the annual cost of caring for and treating individuals with ASD is estimated to be \$35 billion, with a per year family cost of \$67,000 to \$72,000 (Ganz 2006). International lifetime costs per individual have been estimated upwards of \$4 million (US dollars, adjusted for inflation (<u>Järbrink 2001</u>). Further, the majority of people with ASD need treatment throughout life.

There are no evidence-based pharmacotherapies to treat the core symptoms associated with ASD, but advances in treatment continue to be made. Comprehensive treatment programs for young children with ASD vary in both empirical support and presence of recommended components (National Research Council 2001; Odom 2010). The lack of a clear consensus on the superiority of one treatment model has led to children with ASD receiving multiple intervention techniques within home-based programs and/or school-based programs, which are

often lumped together under the term "eclectic". However, though specific program components and characteristics might vary, the importance of early intervention is now well established (National Research Council 2001; Scottish Intercollegiate Guidelines Network 2007), and consensus that early intervention can improve adult outcomes is building. It is now thought that 20% to 25% of individuals with ASD (up from previous estimates of 5%) achieve some level of independence (for example, competitive employment, independent living) (Howlin 2005). However, much remains to be learned about the interaction between intrinsic child characteristics (for example, IQ, chronological age, and severity of symptoms at the start of treatment) and extrinsic factors (for example, the dosage of treatment the children receive, the therapist delivering treatment, and the type of training the therapist received) and their association with the individual's response to treatment. These questions must be addressed if we ultimately want to impact the long-term societal, familial, and personal costs associated with ASD.

1.2 DESCRIPTION OF THE INTERVENTION

A specific form of behavioral intervention, referred to as Early Intensive Behavioral Intervention (EIBI), is one of the more well-established treatments for ASD. Studies using this intervention have demonstrated a reduction in symptom severity, as well as large gains in IQ, adaptive behavior, and language for many, though not all, participants (see Eldevik 2009 and Reichow 2009). EIBI is a highly structured teaching approach for young children with ASD (usually less than five years old), that is rooted in principles of applied behavior analysis (ABA). The origins of EIBI are linked to the University of California at Los Angeles Young Autism Project model (also termed the Lovaas model) (see Lovaas 1981 and Lovaas 1987). The core elements of EIBI involve (a) a specific teaching procedure referred to as discrete trial training, (b) the use of a 1:1 adult-to-child ratio in the early stages of the treatment, and (c) implementation in either home or school settings for a range of 20 to 40 hours per week across one to four years of the child's life (see Eikeseth 2009 and Smith 2010). Typically, EIBI is implemented under the supervision of personnel trained in ABA procedures who systematically follow a treatment manual (for example, Lovaas 1981; Maurice 1996) indicating the scope and sequence of tasks to be introduced and taught. Possible variables affecting child outcomes might be who delivers the treatment (for example, parent, clinician, teacher); treatment intensity and duration (dosage); staff supervision schedules, and intervention settings. Many families of young children receiving treatment, including EIBI, also seek out additional services to address residual symptoms of ASD, such as speech therapy, occupational therapy, or group-based interventions. It is unclear which, if any, of these variables moderate treatment effects.

1.3 HOW THE INTERVENTION MIGHT WORK

There is no standard recommended treatment for ASD. Practice guidelines (for example, Dawson 1997; Volkmar 1999; National Research Council 2001) typically recommend the following treatment components be included in comprehensive programs: (a) addressing the core deficits of autism (for example, social and communication deficits, restricted interests, play skills, imitation); (b) delivering instruction in structured, predictable settings; (c) having a low student-teacher ratio; (d) programming for generalization and maintenance; (e) promoting family involvement; (f) implementing a functional approach to challenging behaviors, and (g) monitoring progress over time.

EIBI includes each of these components. It is initially delivered in one-on-one, highly structured settings (that is, clinic or home) for 25+ hours per week.

Instruction is systematically transferred to natural settings (for example, classroom, school, community) to promote generalization and maintenance. Also, EIBI addresses the core deficits of ASD; individual instructional programs are developed based on the child's current behavioral repertoires (for example, communication and social skills), and a functional approach is used to address challenging behaviors that interfere with learning. Furthermore, EIBI generally includes a family component in that parents implement, manage, or assist in treatment planning and delivery. The specific intervention strategies implemented within EIBI programs include a variety of techniques such as antecedent packages, modelling, use of schedules, and self management. Although EIBI is considered one of the most well-established treatment programs to date for young children with autism, questions remain about the methodology of EIBI research, the essential components and characteristics of EIBI, and non-responders to EIBI.

1.4 WHY IT IS IMPORTANT TO DO THE REVIEW

Early Intensive Behavioral Intervention (EIBI) is the most researched comprehensive intervention program for young children with ASD. As such, it is one of the most frequently requested, recommended, and used treatment programs for these children. Recently five meta-analyses (Eldevik 2009; Reichow 2009; Spreckley 2009; Makrygianni 2010; Virues-Ortega 2010) were published with conflicting results and recommendations for practice. Four of five reviews (Eldevik 2009; Reichow 2009; Makrygianni 2010; Virues-Ortega 2010) concluded EIBI was an effective intervention strategy for many children with ASD, and had weighted mean effect sizes for IQ and adaptive behavior ranging from g = 0.69 to 1.19 and g = 0.42 to 1.09, respectively. The fifth review (Spreckley 2009) concluded EIBI was not superior to standard care, and had effect sizes for IQ and adaptive behavior of g = 0.38 and g = 0.30, respectively. This last review was based on the results of three studies and treated the parent-managed EIBI group of one study (Sallows 2005), which received on average an excess of 30 hours per week of the focal treatment, as

a control group thus negating the positive effects shown in the other two studies. The difference in findings across reviews was likely due to differences in inclusion criteria; only one study (Smith 2000) was included in all of the aforementioned meta-analyses, with the range of included studies being three (Spreckley 2009) to 22 (Virues-Ortega 2010). The extant reviews also used multiple methods of calculating effect sizes, which could also contribute to differences in the findings across studies. The extant meta-analyses considered IQ as the primary outcome, but we feel the intervention is likely to have an equal, if not greater, effect on adaptive (functional) behaviors and therefore it is important to do this review to provide greater clarity of the effects of EIBI on functional behaviors and skills for young children with ASD. Collectively, these discrepant findings have the potential to cause confusion amongst consumers and potentially lead policymakers to misguided decisions and suggest that further reviews are needed to clarify the evidence.

2 Objectives

To systematically review the evidence for the effectiveness of EIBI in increasing functional behaviors and skills for young children with ASD.

3 Methods

3.1 CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

3.1.1 Types of studies

Randomized control trials, quasi-randomized control trials (that is, trials where a quasi-random method of allocation is used, such as alternation or date of birth), and controlled clinical trials (CCTs) comparing EIBI. CCTs will be included when the studies utilizes a multiple-group comparison design in which participants were prospectively identified and assigned to treatment and comparison groups. Given the longitudinal nature of the intervention, we excluded cross-over trials.

3.1.2 Types of participants

Young children with Autistic Disorder, Asperger's Disorder, Pervasive Developmental Disorder, not otherwise specified, or Atypical Autism (APA 1994; WHO 1994) who are younger than six years old at the onset of treatment (that is, all participants within a group must be younger than six years old). Participants were not excluded based on IQ or presence of comorbidities.

3.1.3 Types of interventions

EIBI as defined above, compared with no treatment, with waitlist controls, or treatment as usual (TAU). TAU often combined a variety of treatment components, sometimes referred to as eclectic.

3.1.4 Types of outcome measures

Primary outcomes

- 1. Adaptive behavior
- 2. Psychopathology (symptom severity)
- 3. Deterioration on a primary measure (worsening)

Secondary outcomes

- 1. Intelligence
- 2. Communication and language skills
- 3. Social competence
- 4. Quality of life (for both children with ASD and their caregivers)

Outcomes were measured using standardized assessments, qualitative data (for example, social validity), parent and/or teacher rated scales, and behavioral observation. Due to the likely variability in quality, we considered all measures, which are shown by study in Table 1. Where both parent and teacher measures were used, we prioritised parent reported measures. The parent report measures were consistent across studies; teacher reported measures were not included in all studies.

We grouped outcome time points as follows: immediately post-intervention, one to five months post-intervention, six to 11 months post-intervention, 12 to 23 months post-intervention, 24 to 35 months post-intervention, and so on.

We reported all outcomes in the 'Summary of findings' table.

3.2 SEARCH METHODS FOR IDENTIFICATION OF STUDIES

The search strategy employed sensitivity rather than specificity to avoid missing any potential studies. We did not limit the search by date or language and we did not use a study methods filter.

3.2.1 Electronic searches

We searched the following databases:

Cochrane Central Register of Controlled Trials (CENTRAL), 2011, Issue 4, part of the Cochrane Library, searched 22 November 2011

Ovid MEDLINE (1950 to November Week 2, 2011), searched 22 November 2011

EMBASE (Ovid),1980 to Week 46, 2011, searched 22 November 2011

CINAHL Plus (EBSCOhost), 1937 to current, searched 22 November 2011

PsycINFO (Ovid), 1806 to November Week 3, 2011, searched 22 November 2011

Sociological Abstracts (Proquest),1952 to current, searched 22 November 2011

ERIC (Dialog Datastar), 1966 to current, searched 22 November 2011

Social Science Citation Index (SSCI), 1970 to 22 November 2011, searched 22 November 2011

WorldCat (OCLC), all available years, searched 22 November 2011 metaRegister of Controlled Trials, searched 22 November 2011 Networked Digital Library of Theses and Dissertations (NDLTD), searched 22 The search strategies for each database are in Appendix 1.

3.2.2 Searching other resources

Grey Literature

We searched NDLTD and WorldCat to identify unpublished theses and dissertations not indexed by other databases, and CPCI-SSH to ensure comprehensive coverage of conference literature. We searched mRCT to identify unpublished or ongoing trials.

Reference lists

We searched the reference lists of the studies included in this review and relevant papers to identify additional studies in the published or unpublished literature.

Correspondence

We contacted the authors of the included studies to identify any unpublished or ongoing trials.

3.3 DATA COLLECTION AND ANALYSIS

3.3.1 Selection of studies

Two review authors (BB and KH) independently screened the titles and abstracts yielded by the search against the inclusion criteria listed above. These authors then screened the full text of papers or reports for trials that appear relevant. We sought additional information from the authors of the trials as necessary to resolve questions about the relevance or methodology of a trial. We resolved disagreement about eligibility through discussion, and when disagreements could not be resolved, we sought advice from a mediator (BR or EB). We recorded the reasons for excluding trials, which are shown in Figure 1. Neither of the review authors were blind to the journal titles or to the study authors and institutions.

3.3.2 Data extraction and management

Two review authors (BR and EB) independently extracted data for each trial using a data extraction form to collect information about the population, intervention, randomization methods, blinding, sample size, outcome measures, follow-up duration, attrition and handling of missing data, and methods of analysis. When data were missing, one author (BR) contacted the authors to request additional information. If further information could not be obtained, we coded the variables in question as 'unsure'.

3.3.3 Assessment of risk of bias in included studies

We independently assessed risk of bias using the Cochrane Collaboration tool for assessing risk of bias (<u>Higgins 2008a</u>). We resolved any disagreements by discussion and, if necessary, disagreements were arbitrated by a third party.

We present the risk of bias assessments in a table where the judgment of the review authors (low, high or unclear risk of bias) was followed by a text box providing details on the available information that led to each judgment.

For RCTs, we assessed the following sources of bias: sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective outcome reporting, protection against contamination, baseline measurements, and any other potential sources of bias.

For CCTs, we assessed the following sources of bias: blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective outcome reporting, protection against contamination, baseline measurements, and any other potential sources of bias.

Sequence generation

Was the sequence generation method used adequate? We judged the risk of bias as follows:

'low' when participants were allocated to treatment conditions using randomization such as computer-generated random numbers, a random numbers table, or cointossing;

'unclear' when randomization method was not clearly stated or unknown; 'high' when randomization did not use any of the above methods.

Allocation concealment

Was allocation adequately concealed? We judged the risk of bias as follows: 'low' when participants and researchers were unaware of participants' future allocation to treatment condition until after decisions about eligibility were made and informed consent was obtained;

'unclear' when allocation concealment was not clearly stated or unknown; 'high' when allocation was not concealed from either participants before informed consent or from researchers before decisions about inclusion were made or allocation concealment was not used.

Blinding of participants and personnel

Were participants and personnel blind to which participants were in the treatment

group? We judged the risk of bias as follows:

'low' when blinding of participants and key personnel was ensured;

'unclear' when blinding of participants and key personnel was not reported;

'high' when there was no or incomplete blinding of participants and key personnel or blinding of participants and key personnel was attempted but likely to have been broken.

Blinding of outcome assessment

Were outcome assessors blind to which participants were in the treatment group? We judged the risk of bias as follows:

'low' when blinding of outcome assessment was ensured;

'unclear' when there was not adequate information provided in the study report to determine blinding of outcome assessment, or blinding of outcome assessment was not addressed;

'high' when blinding of outcome assessment was not ensured.

Incomplete outcome data

Did the trial authors deal adequately with missing data? We judged the risk of bias as follows:

'low' when the number of participants randomized to groups is clear and it is clear that all participants completed the trials;

'unclear' when information about which participants completed the study could not be acquired by contacting the researchers of the study;

'high' when there is clear evidence that there was attrition or exclusion from analysis in at least one participant group that is likely related to the true outcome.

Selective outcome reporting

Did the authors of the trial omit to report on any of their outcomes? We judged the risk of bias as follows:

 $'low'\ when\ it\ is\ clear\ that\ the\ published\ report\ includes\ all\ expected\ outcomes;$

'unclear' when it is not clear whether other data were collected and not reported;

'high' when the data from one or more expected outcomes is missing.

Protection against contamination

Could the control group also have received the intervention? We judged the risk of bias as follows:

'low' when allocation was by community, institution, or school and it is unlikely that the control group received the intervention;

'unclear' when professionals were allocated within a clinic or school and it is possible that the communication between intervention and control professionals could have occurred;

'high' when it is likely that the control group received part of the intervention.

Baseline measurements

Were the intervention and control groups similar at baseline? We judged the risk of bias as follows:

'low' when participant performance on outcomes were measured prior to the intervention and no important differences were present across study groups; 'unclear' when no baseline measures of outcome were reported or it was difficult to determine if baseline measures were substantially different across study groups; 'high' when important differences were present and were likely to undermine any post-intervention differences.

Other potential sources of bias

Through assessment, we determined whether any other bias is present in the trial, such as changing methods during the trial, or other anomalies.

3.3.4 Measures of treatment effect

Dichotomous data

We did not locate a study that included dichotomous data. Had such data been included we would have calculated a risk ratio (RR) with a 95% confidence interval (CI) for each outcome in each trial (<u>Higgins 2008a</u>).

Continuous data

We analyzed continuous data when means and standard deviations are presented in the study papers, were made available by the authors of the trials, or were calculable from the available data. No study reported individual data so we were unable to analyze the data to see if it was skewed to correct according to the guidelines outlined in the Cochrane Handbook for Systematic Reviews of Interventions (Deeks 2008, 9.4.5.3). Where similar outcomes were measured using different scales, we calculated a standardized mean difference using Hedges g with small sample correction (Hedges 1985). The meta-analysis combined all three types of effect sizes by transforming all metrics to Hedges g.

3.3.5 Unit of analysis issues

Had data from studies with multiple treatment groups been located we would have analyzed each intervention group separately by dividing the sample size for the common comparator groups proportionately across each comparison (Higgins 2008b, 16.5.5). We did not find cluster-randomized trials; if such trials were found we would have analyzed them in accordance with the methods outlined in the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2008b, 16.3). Details of protocol decisions for the management of unit of analysis issues are shown

3.3.6 Dealing with missing data

We assessed missing data and dropouts in the included studies. We examined the number of missing data collections at post-treatment and reflected this examination in our analysis of the Risk of Bias of incomplete outcome data. For studies with missing data at the post treatment assessment, we conducted analyses using only the available data; that is, we did not impute missing data.

3.3.7 Assessment of heterogeneity

We examined heterogeneity among included studies through the use of the Chi² test, where a low P-value indicated heterogeneity of treatment effects. We also used the I² statistic (Higgins 2002) to determine the percentage of variability that is due to heterogeneity rather than sampling error or chance. We examined estimates of the between studies variance components using τ^2 . We also discussed the possible reasons for any heterogeneity and planned to conduct sensitivity analyses accordingly, where data permitted. We planned to use subgroup analyses to investigate this further, as described below.

3.3.8 Assessment of reporting biases

If we identified 10 or more studies, we would have drawn funnel plots (estimated differences in treatment effects against their standard error). Asymmetry could be due to publication bias, but could also be due to a real relation between trial and effect size, such as when larger trials have lower compliance and compliance is positively related to effect size (Sterne 2008). If such a relation was found, we would have examined clinical variation between the studies (Sterne 2008, 10.4). As a direct test for publication bias, we would have conducted sensitivity analyses to compare the results from published data with data from other sources. However, as we did not identify more than 10 studies, we did not construct a funnel plot. We will do a funnel plot in an update of the review if enough additional trials are located.

3.3.9 Data synthesis

We combined means of the studies by conducting a meta-analysis. Because both RCTs and CCTs were located, we could not combine all studies, thus the meta-analysis was conducted on the four CCTs. We conducted the meta-analyses using a random-effects model due to the possibility of variation in intervention techniques. When meta-analysis was inappropriate, we provided a narrative description of the study results. When narrative descriptions were provided, we were not be able to reach strong conclusions about the effectiveness of EIBI for each outcome.

3.3.10 Subgroup analysis and investigation of heterogeneity

We planned to conduct further investigation of the causes of heterogeneity using subgroup analyses, however, due to the small number of included studies, we

decided subgroup analyses were not appropriate. Further detail and examples of analyses that might be conducted should updates locate more studies are shown in <u>Table 2</u>.

3.3.11 Sensitivity analysis

To explore the impact of studies with high risk of bias on the robustness of the results of the review, we planned to conduct sensitivity analyses by removing studies with a high risk of bias on baseline measurements and blinding of outcome assessment and reanalyzing the remaining studies to determine whether these factors affected the results. However, since we only located a small number of studies, we deemed sensitivity analyses inappropriate. Further detail and example of analyses that might be conducted should updates locate more studies are shown in Table 2.

4 Results

4.1 DESCRIPTION OF STUDIES

See: Characteristics of included studies; Characteristics of excluded studies.

4.1.1 Results of the search

Figure 1 shows a flow diagram of search results. We conducted electronic searches in November 2011, returning a total of 6801 records after deduplication. Initial screening reduced the number of papers to 55 potential studies. The full papers of these 55 studies were evaluated. Five studies were suitable for inclusion; 41 were excluded because they were not RCTs or CCTs (for example, retrospective studies); seven were excluded because the comparison group was not treatment as usual (instead varying intensities of EIBI were compared); and two were excluded because some participants were age six or older. No additional studies were identified in the search of reference lists. There are no ongoing studies that we are aware of.

4.1.2 Included studies

Five studies examining EIBI for young children with ASD are included in this review (Smith 2000; Howard 2005; Cohen 2006; Magiati 2007; Remington 2007).

Cohen 2006 used a prospective CCT design to compare two groups of children with autism (that is, 21 children who received 35 to 40 hours of EIBI and 21 children who received treatment as usual (TAU) - eclectic treatment provided by the local public school). Assignment to groups was based on parent preferences. Independent examiners assessed outcomes at treatment entry and one, two and three years after treatment entry. The EIBI group obtained significantly higher IQ and adaptive behavior scores. Further, more children from the EIBI group (17) were fully included or included with support into regular education classrooms than children from the comparison group (1).

Howard 2005 used a prospective CCT design to compare two groups of children with autism (that is, 29 children who received 25 to 30 hours of EIBI and 16 children who received TAU - autism specific programming provided by the local public school). Assignment to groups was made by the child's IFSP or IEP teams and heavily based on parent preferences. Independent examiners assessed outcomes at treatment entry and 14 months after treatment entry. The EIBI group obtained

significantly higher IQ, language, and adaptive behavior scores at post-test. Further, learning rates were higher for children in the treatment group.

Magiati 2007 used a prospective CCT design to compare two groups of children with autism (that is, 28 children who received more than 30 hours of EIBI and 16 children who received TAU - autism specific preschool programming). Assignment to groups was based on parent preferences. The first author and a research assistant assessed outcomes at treatment entry and 24 months after treatment entry. There were no statistically significant differences at post-treatment between the two groups on IQ, language, play, adaptive behavior, or autism severity.

Remington 2007 used a prospective CCT design to compare two groups of children with autism (that is, 23 children who received more than 25 hours of EIBI and 21 children who received TAU - autism specific programming provided by public schools). Assignment to groups was based on parent preferences. Outcomes were assessed at treatment entry and 24 months after treatment entry. The EIBI group obtained significantly higher scores on measures of IQ, language, adaptive behavior, and positive social behavior at post-test. Further, measures of parent wellbeing indicated no increased stress or problems for families in EIBI group.

Smith 2000 used a RCT design to compare two groups of children with autism (that is, 15 children who received an average of 24 hours of EIBI and 13 children who received autism-specific parent training). Assessors who were blind to group assignment and treatment history assessed outcomes at treatment entry and when children were seven to eight years old. The EIBI group obtained significantly higher scores on measures of IQ, visual-spatial skills, language, and academic skills. No differences were noted between groups on measures of adaptive behavior or behavior problems.

4.1.3 Study location

Three of five studies (Smith 2000; Howard 2005; Cohen 2006) were conducted in the United States. Two of five studies (Magiati 2007; Remington 2007) were conducted in the United Kingdom.

4.1.4 Study design

One study (<u>Smith 2000</u>) used a RCT design, in which participants were randomized to EIBI or treatment as usual. Four of five studies (<u>Howard 2005</u>; <u>Cohen 2006</u>; <u>Magiati 2007</u>; <u>Remington 2007</u>) used a CCT design. We located no quasirandomized control trials.

4.1.5 Participants

The five studies included a total of 203 children; 116 children in the EIBI groups and 87 children in the TAU groups. Across all fives studies the mean chronological age at treatment entry ranged from 30.2 to 42.5 months. All studies had an inclusion

criterion that the participants have an independent ASD diagnosis; four of the five studies specified children could have a diagnosis of autistic disorder or PDD-NOS. The diagnoses of ASD were further confirmed in three of the five studies by using the ADI-R. All studies specified that children could not have any other major medical conditions that would interfere with participation in the treatment. Two studies specified an IQ inclusion criterion. In Smith 2000 children with autism had to have an IQ of 35 to 75 at treatment entry; in Cohen 2006 children with autism had to have an IQ of greater than 35. Across studies the mean pre-treatment IQs ranged from 30.9 to 83.0 for children in the treatment groups and 37.4 to 65.0 for children in the comparison groups. Three of the five studies included a residency inclusion criterion for participants (for example, children had to live within 60 miles of treatment center) (Smith 2000; Cohen 2006; Remington 2007). Two of the five studies specified children could not have or currently be participating in other interventions (Howard 2005; Magiati 2007).

4.1.6 Interventions

The duration of the EIBI treatment ranged from 14 months to 36 months. Across studies, the mean duration of treatment for children in the EIBI group was 26.3 months. The intensity of treatment was greater than 24 hours per week across all five studies. Four of the five studies reported using EIBI based on Lovaas (Lovaas 1993)/UCLA Young Autism Project model. One study (Howard 2005) reported using EIBI based on Maurice and colleagues (Maurice 1996; Maurice 2001).

4.1.7 Comparisons

The comparison group in four studies consisted of TAU provided by public schools (Howard 2005; Cohen 2006; Magiati 2007; Remington 2007), and one consisted of parent training (Smith 2000). Three studies reported that public school treatment was eclectic or autism specific (Howard 2005; Magiati 2007; Remington 2007). In Cohen 2006 the comparison group received eclectic general programming for children with special needs provided by the public school system.

4.1.8 Excluded studies

We examined 50 full papers of studies that were excluded from this review. The main reason for exclusion was the use of study designs other than RCTs or CCTs (primarily retrospective studies) (see Figure 1). Select characteristics of key excluded studies are shown in the Characteristics of excluded studies. The studies that are shown were chosen because they were either a seminal study (Lovass 1987), a study that has led to misinterpretation of results in previous systematic reviews (Sallows 2005), or a study for which we received inquiry about from authors of included studies who were contacted for additional studies as part of our search strategy (Eikeseth 2007).

4.2 RISK OF BIAS IN INCLUDED STUDIES

4.2.1 Allocation

One study (Smith 2000) was conducted using a randomized design, thus has a lower risk of selection bias than the other four studies (Howard 2005; Cohen 2006; Magiati 2007; Remington 2007), which were conducted using non-randomized assignment to groups. In all four non-randomized studies, parent preference was the main method by which participants were allocated to groups.

4.2.2 Blinding

4.2.3 Participants and personnel (performance)

Due to the nature of the intervention, in which participants and study personnel interact with high frequency and regularity, risk of bias from lack of blinding of participants and study personnel was high for all five studies.

4.2.4 Outcome assessors (detection bias)

There was a high risk of detection bias in all studies. For all studies, the primary outcome was assessed using parent report and in one study (<u>Magiati 2007</u>), outcome assessors for the remaining measures were not blind to treatment status.

4.2.5 Incomplete outcome data

Risk of bias from incomplete outcome data was low for four studies. One study (<u>Howard 2005</u>) reported 8 of 37 (22%) participants receiving EIBI did not complete post-treatment assessment.

4.2.6 Selective reporting

Risk of bias from selective reporting was low for all five studies.

4.2.7 Other potential sources of bias

4.2.8 Protection against contamination

Risk of bias from contamination of the comparison groups receiving EIBI was low in all five studies.

4.2.9 Baseline measurements

The risk of important differences between groups before treatment was low in two studies (Smith 2000; Cohen 2006) and high in the remaining three studies (Howard 2005; Magiati 2007; Remington 2007). In Howard 2005 and Remington 2007 studies, on average, the EIBI group was significantly younger than the TAU group at intake (30.9 to 37.4 months, P = 0.0003; 35.7 to 38.4 months, P < 0.05,

respectively). In the <u>Magiati 2007</u> study, on average, the EIBI group had significantly higher IQ scores than the TAU group at time 1 measurement (83.0 to 65.2, P = 0.04), and significantly higher standardized scores on the Vineland Composite (59.6 to 55.4, P = 0.04) and Vineland Socialization subscale (60.3 to 56.6, P = 0.05).

4.3 EFFECTS OF INTERVENTIONS

See: Summary of findings for the main comparison Early intensive behavioral intervention for increasing functional behaviors and skills for young children with autism spectrum disorders (ASD); Summary of findings 2 Early intensive behavioral intervention for decreasing psychopathology and symptom severity for young children with autism spectrum disorders (ASD); Summary of findings 3 Early intensive behavioral intervention for increasing intelligence and cognition for young children with autism spectrum disorders (ASD); Summary of findings 4 Early intensive behavioral intervention for increasing communication and language skills for young children with autism spectrum disorders (ASD); Summary of findings 5 Early intensive behavioral intervention for increasing social competence and skills for young children with autism spectrum disorders (ASD); Summary of findings 6 Early intensive behavioral intervention for increasing quality of life for young children with autism spectrum disorders (ASD)

4.3.1 Adaptive behavior

All studies reported outcome data on adaptive behavior using the Vineland Adaptive Behavior Scales Adaptive Behavior Composite (Sparrow 1984). The results of the four CCT studies (Howard 2005; Cohen 2006; Magiati 2007; Remington 2007) were synthesized in a random-effects meta-analysis using the standardized mean difference effect size with small sample correction (Hedges 1985). The weighted mean effect size for difference in adaptive behavior between treatment and comparison groups was g = 0.69 (95% CI 0.38 to 1.01; P < 0.0001). To assess the clinical significance of this effect size, we examined the raw scores reported by Remington 2007, which showed that children receiving EIBI had, on average, up to 20 more adaptive behaviors than children receiving TAU. We assessed heterogeneity using the Q-statistic (Q(3) = 2.49, P = 0.37), I^2 (0%), and τ^2 (0.0). These measures of heterogeneity suggest the results were homogeneous and do not support examination of moderators. The effect of EIBI on adaptive behavior for the one study conducted using a randomized design (Smith 2000) was g = 0.14, which is considerably less than the combined effects of the CCTs. The effect of EIBI on adaptive behavior for the included studies is shown in Figure 2. Syntheses of the three domains of the Vineland (Communication, Socialization, and Daily Living Skills) are reported in the language, social competence, and quality of life sections, respectively, below.

4.3.2 Psychopathology (symptom severity)

Psychopathology was reported in three studies (Smith 2000; Magiati 2007; Remington 2007). However, due to the use of measures not designed as outcome measures (ADI-R and ASQ) and measurement across different constructs (for instance, autism symptoms, problem behavior), we decided not to statistically synthesize data on psychopathology. Magiati 2007 measured symptom severity using the Autism Diagnostic Interview-Revised (ADI-R; Lord 1994). Their results suggest that children receiving EIBI had similar autism symptoms after treatment (g = 0.45; 95% CI -0.18-1.09; P = .16). Remington 2007 measured symptom severity using the Autism Screening Questionnaire (Berument 1999), which was derived from the ADI-R, and the Developmental Behavior Checklist Autism Algorithm (Einfeld 2002). After averaging the father and mother ratings, their results showed that children receiving EIBI had similar levels of autism symptoms and problem behavior after treatment than children in the TAU group (g = 0.23; 95% CI -0.41 to 0.87; P = 0.48) and (g = 0.59; 95% CI -0.06 to 1.24; P = 0.06), respectively. The Developmental Behavior Checklist also produces a total score of problem behavior, which showed the children receiving EIBI in Remington 2007 had similar problem behaviors than children receiving TAU (g = 0.57; 95% CI -0.08 to 1.22; P = 0.06). Smith 2000 measured psychopathology using the Child Behavior Checklist (Achenbach 1991). After averaging all reported subscales, their results showed that children receiving EIBI had similar levels of socioemotional problems than children receiving TAU as reported both by parents (g = 0.2395% CI -0.52 to 0.97; P = 0.54) and teachers (g = 0.14; 95% CI -0.60 to 0.88; P = 0.72).

4.3.3 Adverse events (deterioration on a primary outcome)

No deterioration on primary outcome measures or adverse events were reported as a result of treatment in any study.

4.3.4 Intelligence

Intelligence (IQ) was measured in all studies, although the specific IQ tests used varied across and within studies (see <u>Table 1</u>). The results of the four CCT studies (<u>Howard 2005</u>; <u>Cohen 2006</u>; <u>Magiati 2007</u>; <u>Remington 2007</u>) were synthesized in a random-effects meta-analysis using the standardized mean difference effect size with small sample correction (<u>Hedges 1985</u>). The weighted mean effect size for difference in IQ between the treatment and comparison groups was g = 0.76 (95% CI 0.40 to 1.11; P < 0.0001), which translates to an difference of 11 points on standardized IQ tests; that is, on average, children receiving EIBI had IQs that were 11 points higher than children receiving TAU. We assessed heterogeneity using the Q-statistic (Q(3) = 3.79, P = 0.28), I^2 (21%), and τ^2 (0.03). These measures of heterogeneity suggest the results were homogeneous and do not support examination of moderators. The effect of EIBI on IQ for the one study conducted using a randomized design (<u>Smith 2000</u>) was g = 0.74, which is nearly identical to the combined effects of the CCTs. The effect of EIBI on IQ for the included studies is

4.3.5 Communication and language skills

Three studies (Cohen 2006; Magiati 2007; Remington 2007) measured the effects of EIBI on expressive and receptive language using the Reynell Developmental Language Scales (Reynell 1990). The results of the three studies were synthesized in a random-effects meta-analysis using the standardized mean difference effect size with small sample correction (Hedges 1985). The weighted mean effect size for difference in expressive language between the treatment and comparison group was g = 0.50 (95% CI 0.05 to 0.95; P = 0.03). We assessed heterogeneity using the Qstatistic (Q(2) = 3.01, P = 0.22), I^2 (3.4%), τ^2 (0.05). The weighted mean effect size for difference in receptive language between the treatment and comparison group was g = 0.57 (95% CI 0.20 to 0.94; P = 0.03). We assessed heterogeneity using the Q-statistic (Q(2) = 1.96, P = .37), I^2 (0%), and τ^2 (0.0). All measures of heterogeneity suggest the results were homogeneous and do not support examination of moderators. The effect of EIBI on expressive and receptive language for the one study conducted using a randomized design (Smith 2000) was g = 0.36 and g =0.48, respectively, which is similar to the combined effects of the CCTs. The effect of EIBI on expressive language in the included studies is shown in Figure 4 and the effect on receptive language is shown in Figure 5.

Participant's daily communication skills were also measured using the Vineland Adaptive Behavior Scales Communication domain (Sparrow 1984). The results of the four CCT studies (Howard 2005; Cohen 2006; Magiati 2007; Remington 2007) were synthesized in a random-effects meta-analysis using the standardized mean difference effect size with small sample correction (Hedges 1985). The weighted mean effect size for difference in communication skills between treatment and comparison groups was g = 0.74 (95% CI 0.30 to 1.18; P = .0009). We assessed heterogeneity using the Q-statistic (Q(3) = 5.68, P = 0.13), I² (47%), and τ^2 (0.09). Although there appears to be evidence of possible heterogeneity between studies, the small sample size precludes our ability to examine moderators. The effect of EIBI on daily communication skills for the one study conducted using a randomized design (Smith 2000) was g = 0.30, which is much lower than the combined effects of the CCTs. The effect of EIBI on everyday communication skills for the included studies is shown in Figure 6.

4.3.6 Social competence

Participants' daily socialization skills were also measured using the Vineland Adaptive Behavior Scales Socialization domain (Sparrow 1984). The results of the four CCT studies (Howard 2005; Cohen 2006; Magiati 2007; Remington 2007) were synthesized in a random-effects meta-analysis using the standardized mean difference effect size with small sample correction (Hedges 1985). The weighted mean effect size for difference in social competence between treatment and comparison groups was g=0.42 (95% CI 0.11 to 0.73; P=0.0008). We assessed

heterogeneity using the Q-statistic (Q(3) = 1.45, P = .69), I² (0%), and τ^2 (0.0). All measures of heterogeneity suggest the results were homogeneous and do not support examination of moderators. The effect of EIBI on social competence for the one study conducted using a randomized design (Smith 2000) was g = -0.12, which is much lower than the combined effects of the CCTs. The effect of EIBI on everyday social competence for the included studies is shown in Figure 7. Remington 2007 also measured prosocial behavior using the Nisonger Child Behavior Rating Form-Positive Social Behavior subscale (Aman 1996). After averaging across mother and father informants, their study showed children receiving EIBI had similar social skills to children who received TAU (g = 0.47; 95% CI -0.13 to 1.07; P = 0.12).

4.3.7 Quality of life

There were multiple measures of quality of life in the studies included in this review. Five studies reported on each domain of the Vineland (Sparrow 1984) including daily living skills, which we have classified as an indicator of quality of life. The results of the four CCT studies (Howard 2005; Cohen 2006; Magiati 2007; Remington 2007) were synthesized in a random-effects meta-analysis using the standardized mean difference effect size with small sample correction (Hedges 1985). The weighted mean effect size for difference in daily living skills between the treatment and comparison groups was g = 0.55 (95% CI 0.24 to 0.87; P = 0.0005). We assessed heterogeneity using the Q-statistic (Q(3) = 1.61, P = 0.66), I^2 (0%), and τ^2 (0.0). All measures of heterogeneity suggest the results were homogeneous and do not support examination of moderators. The effect of EIBI on daily living skills for the one study conducted using a randomized design (Smith 2000) was g = -0.03, which is much lower than the combined effects of the CCTs. The effect of EIBI on daily living skills for the included studies is shown in Figure 8.

Two studies (Smith 2000; Cohen 2006) provided quality of life data pertaining to academic placement (that is, percentage of time spent with typical peers). Cohen 2006 reported that 17 of 21 children receiving EIBI and 1 of 21 children receiving TAU were included in general education settings (6 of 17 full inclusion without assistance, 4 of 17 some paraprofessional support, and 6 of 17 with full time paraprofessional support). Smith 2000 reported that 6 of 15 children receiving EIBI and 3 of 13 children receiving TAU were included in general education settings (4 of 6 full inclusion without assistance, 2 of 6 partial inclusion with paraprofessional support).

One study (Remington 2007) reported data on parental wellbeing. Specifically, they reported data on parental stress using the Questionnaire on Resources and Stress-Friedrich (Friedrich 1983), parental anxiety and depression using the Hospital Anxiety and Depression Scale (Zigmond 1983), and on parental positive perceptions using the Kansas Inventory of Parental Perceptions-Positive Contributions scale (Behr 1992). After averaging across mothers and fathers, the results from their study show that parents of children receiving EIBI had similar levels of stress compared to

parents of children receiving TAU (g = 0.26; 95% CI -0.33 to 0.86; P = 0.38), similar levels of anxiety and depression (g = 0.11; 95% CI = -0.48 to 0.70; P = 0.71), and similar levels of positive perceptions (g = -0.28; 95% CI -0.87 to 0.32; P = 0.36). Reported in Remington 2007 but masked here by our decision to average mothers and fathers was a finding that fathers of children in the EIBI group reported more depression than fathers with children in the TAU group.

5 Discussion

5.1 SUMMARY OF MAIN RESULTS

We identified five studies comparing the effects of EIBI to TAU in young children with ASD. One study (Smith 2000) used a RCT design; four studies (Howard 2005; Cohen 2006; Magiati 2007; Remington 2007) used a CCT design. We conducted meta-analyses using a random-effects model on the four studies using a CCT design on adaptive behavior composite, IQ, communication and language skills, social competence, and daily living skills. The results show evidence that EIBI improves adaptive behavior (SMD ES 0.69), IQ (SMD ES 0.76), expressive and receptive language (SMD ES 0.50, SMD ES 0.57, respectively), everyday communication skills (SMD ES 0.74), everyday social competence (SMD ES 0.34), and daily living skills (SMD ES 0.47) for this population. Additional measures of psychopathology and quality of life were reported but we chose not to conduct meta-analysis on these outcomes since multiple measures were used across studies. We rated the quality of the evidence as Low using the Grade system, which means that more research could very well change the estimate of the effect and our confidence that it is precise, therefore results should be considered with caution. In addition, four of the studies used a CCT design, and in three of those studies there was group imbalance on baseline measures. Thus, the results must be interpreted with caution because of risk of bias.

5.2 OVERALL COMPLETENESS AND APPLICABILITY OF EVIDENCE

The number of studies meeting our inclusion criteria was few; more studies examining EIBI for children with ASD were excluded than were included. There was only one RCT investigating the use of EIBI with young children with ASD. Several factors impact the completeness and applicability of these findings. The reliance on four CCT studies with three of those showing group imbalance limits the internal validity of those studies and makes it difficult to draw firm conclusions about the strength of EIBI. The inclusion criteria relating to the age of the participants (that is, all participants age five or under) limits the generalizability of the results to older children. In addition, effects may not be generalizable to young children with significant intellectual impairments, as the floor effect of the IQ measures in several of the studies may have limited the accuracy of the sample characterization. The lack

of a standardized control group also limits the generalization of results, as TAU conditions varied in intensity, duration, and intervention strategies implemented. Finally, intervention effects related to psychopathology, quality of life (that is, caregiver mental health, classroom placement), and community functioning (that is, participation in community events/activities) were not included in all studies and/or were not measured in a standardized way that allowed for meta-analysis. Outcomes related to these domains are of increased importance and will allow for greater generalizability of findings. Additional research using rigorous methods, standardized control groups, and measures that accurately capture quality of life and functioning across environments is needed before additional generalizations and recommendations about who will benefit most from EIBI and the effects of EIBI on quality of life and everyday functioning can be made with confidence.

5.3 QUALITY OF THE EVIDENCE

The quality of the evidence, as rated by the GRADE software, is low and is shown in the 'Summary of findings' tables. This rating reflects the use of non-randomized trials, serious concerns with risk of bias, imprecision due to small sample sizes, and publication bias, which cannot be ruled out. Given the nature of the intervention and the selected outcome measures, the risk of performance and detection bias are high. Intervention providers and the children's parents were aware of treatment status. Parental interview was the method of data collection for the primary outcome measure (Vineland Adaptive Behavior Scales; Sparrow 1984). Although the Vineland is commonly used and is a standardized measure, parent report is not considered the most reliable method of measurement, which is further compounded because parents were aware, and in most cases chose the treatment status. Given this high risk of bias, the results should be interpreted cautiously. The risk of publication bias is unclear since it could not be assessed due to the small number of studies included in the review.

5.4 POTENTIAL BIASES IN THE REVIEW PROCESS

Our decision to include four non-randomized studies and three of those studies having group imbalance increases the risk of bias for the review, as indicated by the low quality rating assigned using the GRADE software. Other potential sources of bias include our decision to exclude studies using geographically-based comparisons between EIBI and TAU.

5.5 AGREEMENTS AND DISAGREEMENTS WITH OTHER STUDIES OR REVIEWS

The results of this review are consistent with most meta-analyses of EIBI (Eldevik 2009; Reichow 2009; Makrygianni 2010; Virues-Ortega 2010), which show positive effects in favor of EIBI for IQ and adaptive behavior. Our review differs from the one

meta-analysis showing no effect for EIBI (<u>Spreckley 2009</u>) by our exclusion of <u>Sallows 2005</u>, which <u>Spreckley 2009</u> included and treated the parent-mediated EIBI group as a control group for their analysis. Our review also differs from previous meta-analyses with our selection of adaptive behavior as the primary outcome; all previous reviews used IQ as the primary outcome. Our review extends the knowledge of the effects of EIBI through the inclusion of additional outcomes such as psychopathology, communication and language skills, and quality of life.

6 Authors' Conclusions

6.1 IMPLICATIONS FOR PRACTICE AND POLICY

There is some evidence that EIBI is an effective treatment for children diagnosed with an ASD. The evidence points to gains in the areas of IQ, adaptive behavior, socialization, communication, and daily living skills, with the largest gains made in IQ and the smallest in socialization. The primary issue is that the quality of the evidence to support the use of EIBI is quite limited, that is, we only have evidence from a handful of studies that are not of the optimum design. Only one study used a RCT design and across studies there were small sample sizes. We strongly recommend that decisions about the use of EIBI for children with ASD be made on a case by case basis. It is important that providers of EIBI are aware of the limited quality of the current evidence and use clinical decision-making guidelines, such as seeking the family's input and drawing upon prior clinical experience, when making recommendations to clients on the use EIBI.

6.2 IMPLICATIONS FOR RESEARCH

The present review does add to the growing evidence base that EIBI is an effective treatment for children with ASD (Lovaas 1987; Eldevik 2009; Reichow 2009). However, the quality of the evidence is of concern. Future studies should employ RCT designs and larger sample sizes, when feasible. There are specific issues that warrant further study. The impact of EIBI on parental health and wellbeing, as well as a family's overall quality of life is an area for future inquiry, as research indicates that parental factors such as stress can impact children's response to treatment (Osborne 2007). More research is needed to determine child or parent variables that predict which children will or will not respond to treatment. The inclusion of biomarkers or physiological measures, such as EEG, may provide insight into biologically-relevant variables that predict treatment response. Finally, comparative effectiveness studies are needed to determine if EIBI is more effective than other active treatments recommended for children with ASD. We also recommend that intervention scientists examining the efficacy of EIBI establish guidelines for the minimum number of hours per week children must receive EIBI, and a core set of outcome measures that can be used across researchers. Further, researchers should more clearly delineate the active ingredients of EIBI under study, and describe the educational or behavioral practices participants in the control group use as well as

the degree to which those practices overlap with the treatment group. \\

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* Indicates the major publication for the study

9 Summary of findings tables

9.1 SUMMARY OF FINDINGS TABLE 1: FOR THE MAIN COMPARISON. [EXPLANATION]

Early intensive behavioral intervention for increasing functional behaviors and skills for young children with autism spectrum disorders (ASD)

Patient or population: Young children with ASD

Settings: Home

Outcomes	Illustrative comparative risks* (95% Cl)	Relative effect (95% CI)	No of Participants	Quality of the evidence	Comments
	Assumed risk	Corresponding risk		(studies)	(GRADE)	
	Control	Early Intensive Behavioral Intervention				
Adaptive behavior (composite) Vineland Adaptive Behavior Scales Follow-up: 1-3 years	The mean adaptive behavior composite score in the control groups was 0.36 standard deviations lower at post-treatment compared to pre-treatment (0.78 lower to 0.05 higher) ^{1,2}	The mean adaptive behavior composite score in the intervention groups was 0.69 standard deviations higher (0.38 to 1.01 higher) ³		171 (5 studies ⁴)	⊕⊕⊖⊝ low ^{5,6}	

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

¹ This is a difference in standard deviations calculated for the TAU group from change scores before and after the intervention period.

² Relative effect for TAU calculated on pre-post change for control groups from Cohen, Howard, and Magiati studies (Remington excluded because only raw scores were reported).

³ This is a difference between standard deviations.

⁴ Four CCTs and one RCT.

⁵ Risk of bias assessment shows mostly equal levels of low risk and high risk. High risk items include allocation concealment, participants and personnel not being blind to treatment status, outcome assessors not being blind to treatment status, and significant differences on key variables at baseline measurement.

⁶ Small number of included studies precludes our ability to examine funnel plot and thereby cannot exclude the potential of publication bias.

9.2 SUMMARY OF FINDINGS TABLE 2

Early intensive behavioral intervention for decreasing psychopathology and symptom severity for young children with autism spectrum disorders (ASD)

Patient or population: Young children with ASD

Settings: Home

Outcomes	Illustrative comparative risks* (95% C	1)	Relative effect (95% CI)	No of Participants	Quality of the evidence	Comments
	Assumed risk	Corresponding risk		(studies)	(GRADE)	
	Control	Early Intensive Behavioral Intervention				
Symptom severity Autism diagnostic instruments and screeners ¹ Follow-up: 1-3 years	See comment ²	See comment		70 (2 studies³)	⊕⊕⊖⊖ low ^{4,5}	

Standardized behavior checklists ⁶	The mean problem behavior score in the control groups was 0.28 standard deviations lower at post-treatment compared to pre-treatment ⁷	The mean problem behavior score in the intervention groups was 0.57 standard deviations lower (1.24 lower to 0.06 higher) ⁸		39 (2 studies ⁹)	⊕⊕⊖⊝ low ^{4,5}	
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^{*}The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

¹ Autism Diagnostic Interview-Revised, Autism Screening Questionnaire, Developmental Behavior Checklist-Autism Algorithm.

² This is a difference in standard deviations calculated for the TAU group from change scores before and after the intervention period.

³ Magiati 2007; Remington 2007.

⁴ Risk of bias assessment shows mostly equal levels of low risk and high risk. High risk items include allocation concealment, participants and personnel not being blind to treatment status, outcome assessors not being blind to treatment status, and significant differences on key variables at baseline measurement.

⁵ Small number of included studies precludes our ability to examine funnel plot and thereby cannot exclude the potential of publication bias.

- ⁶ Developmental Behavior Checklist, Child Behavior Checklist.
- ⁷ This is a difference in standard deviations calculated for the TAU group from change scores before and after the intervention period for the Remington study on the Developmental Behavior Checklist Problem Behavior Scale (Smith 2000 only reported data on the Child Behavior Checklist at post-treatment).
- ⁸ SMD calculated using data from the Remington study on the Developmental Behavior Checklist Problem Behavior Scale (Smith 2000 only reported data on the Child Behavior Checklist at post-treatment).
- 9 Remington 2007; Smith 2000.

9.3 SUMMARY OF FINDINGS TABLE 3

Early intensive behavioral intervention for increasing intelligence and cognition for young children with autism spectrum disorders (ASD)

Patient or population: Young children with ASD

Settings: Home

Outcomes	Illustrative comparative risks* (95% CI)	Relative effect (95% CI)	No of Participants	Quality of the evidence	Comments
	Assumed risk	Corresponding risk		(studies)	(GRADE)	
	Control	Early Intensive Behavioral Intervention				
IQ Standardized tests of intelligence Follow-up: 1-3 years	The mean IQ in the control groups was 0.30 standard deviations higher at post-treatment compared to pretreatment (0.03 lower to 0.63 higher) ¹	The mean IQ in the intervention groups was 0.76 standard deviations higher (0.4 to 1.11 higher) ²		172 (5 studies³)	⊕⊕⊖⊝ low ^{4,5}	

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

¹ This is a difference in standard deviations calculated for the TAU group from change scores before and after the intervention period

² This is a difference between standard deviations

³ Four CCTs and one RCT

⁴ Risk of bias assessment shows mostly equal levels of low risk and high risk. High risk items include allocation concealment, participants and personnel not being blind to treatment status, and significant differences on key variables at baseline measurement

⁵ Small number of included studies precludes our ability to examine funnel plot and thereby cannot exclude the potential of publication bias

9.4 SUMMARY OF FINDINGS TABLE 4

Early intensive behavioral intervention for increasing intelligence and cognition for young children with autism spectrum disorders (ASD)

Patient or population: Young children with ASD

Settings: Home

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants	Quality of the evidence	Comments
	Assumed risk	Corresponding risk		(studies)	(GRADE)	
	Control	Early Intensive Behavioral Intervention				
Expressive Language Reynell Follow-up: 1-3 years	The mean expressive language in the control groups was 0.14 standard deviations higher at post-treatment compared to pre-treatment (0.57 lower to 0.84 higher) ¹	The mean expressive language in the intervention groups was 0.50 standard deviations higher (0.05 to 0.95 higher) ²		124 (4 studies ³)	⊕⊕⊖⊝ low ^{4,5}	SMD 0.5 (0.05 to 0.95)

Reynell	The mean receptive language in the control groups was 0.26 standard deviations higher at post-treatment compared to pre-treatment (0.45 lower to 0.97 higher) ^{1,6}	The mean receptive language in the intervention groups was 0.57 standard deviations higher (0.2 to 0.94 higher) ²	124 (4 studies³)	⊕⊕⊖⊖ low ^{4,5}	SMD 0.57 (0.2 to 0.94)
VABS Communication Domain Vineland Adaptive Behavior Scales Follow-up: 1-3 years	The mean VABS communication domain in the control groups was 0.05 standard deviation units lower at post-treatment compared to pre-treatment (0.43 lower to 0.34 higher) ^{1,7}	The mean VABS communication domain in the intervention groups was 0.74 standard deviations higher (0.3 to 1.18 higher) ²	171 (5 studies ⁸)	⊕⊕⊖⊝ low ^{4,5}	SMD 0.74 (0.3 to 1.18)

^{*}The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

- ¹ This is a difference in standard deviations calculated for the TAU group from change scores before and after the intervention period.
- ² This is a difference between standard deviations
- ³ 3 CCT (Cohen 2006, Howard 2005, Magiati 2007) and 1 RCT
- ⁴ Risk of bias assessment shows mostly equal levels of low risk and high risk. High risk items include allocation concealment, participants and personnel not being blind to treatment status, outcome assessors not being blind to treatment status, and significant differences on key variables at baseline measurement
- ⁵ Small number of included studies precludes our ability to examine funnel plot and thereby cannot exclude the potential of publication bias
- ⁶ Relative effect for TAU calculated on pre-post change for control groups from Howard (Cohen and Magiati studies excluded because only raw scores were obtained or reported).
- ⁷ Relative effect for TAU calculated on pre-post change for control groups from Cohen, Howard, and Magiati studies (Remington excluded because only raw scores were reported).
- 8 4 CCT and 1 RCT

9.5 SUMMARY OF FINDINGS TABLE 5

Early intensive behavioral intervention for increasing social competence and skills for young children with autism spectrum disorders (ASD)

Patient or population: Young children with ASD

Settings: Home

Outcomes	Illustrative comparative risks* (95% CI) Assumed risk	Corresponding risk	Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Control	Early Intensive Behavioral Intervention				
VABS Socialization Domain Vineland Adaptive Behavior Scales Follow-up: 1-3 years	the control groups was 0.00 standard deviations higher at post-treatment compared to pre-treatment (0.38 lower	The mean VABS socialization domain in the intervention groups was 0.42 standard deviations higher (0.11 to 0.73 higher) ³		171 (5 studies ⁴)	⊕⊕⊖⊝ low ^{5,6}	SMD 0.42 (0.11 to 0.73)

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

¹ This is a difference in standard deviations calculated for the TAU group from change scores before and after the intervention period.

² Relative effect for TAU calculated on pre-post change for control groups from Cohen, Howard, and Magiati studies (Remington excluded because only raw scores were reported).

³ This is a difference between standard deviations

^{4 4} CCT and 1 RCT

⁵ Risk of bias assessment shows mostly equal levels of low risk and high risk. High risk items include allocation concealment, participants and personnel not being blind to treatment status, outcome assessors not being blind to treatment status, and significant differences on key variables at baseline measurement

⁶ Small number of included studies precludes our ability to examine funnel plot and thereby cannot exclude the potential of publication bias

9.6 SUMMARY OF FINDINGS TABLE 6

Early intensive behavioral intervention for increasing quality of life for young children with autism spectrum disorders (ASD) and their parents

Patient or population: Young children with ASD

Settings: Home

Outcomes	Illustrative comparative risks* (95% CI) Assumed risk	Corresponding risk	Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Control	Early Intensive Behavioral Intervention				
VABS Daily Living Skills Vineland Adaptive Behavior Scales Follow-up: 1-3 years	The mean VABS daily living skills in the control groups was 0.54 standard deviations lower for control group at post-treatment compared to pretreatment (1.22 lower to 0.31 higher) ^{1,2}	The mean VABS daily living skills in the intervention groups was 0.55 standard deviations higher (0.24 to 0.87 higher) ³		171 (5 studies ⁴)	⊕⊕⊖⊖ low ^{5,6}	SMD 0.55 (0.24 to 0.87)

Parental Stress Questionnaire on Resources and Stress Friedrich- short form Follow-up: mean 2	The mean parental stress in the control groups was 0.37 standard deviations higher at post-treatment compared to pre-treatment (0.23 lower to 0.98 higher) ¹	The mean parental stress in the intervention groups was 0.26 standard deviations higher (0.33 lower to 0.86 higher) ³	44 (1 study ⁷)	⊕⊕⊖⊝ low ^{5,6}
Parental Anxiety and Depression Hospital Anxiety and Depression Scale Follow-up: mean 2 years	The mean parental anxiety and depression in the control groups was 0.24 standard deviations lower at post-treatment compared to pretreatment ¹	The mean parental anxiety and depression in the intervention groups was 0.11 standard deviations higher (0.48 lower to 0.7 higher) ³	44 (1 study ⁷)	⊕⊕⊖⊝ low ^{5,6}
Parental Positive Perceptions Kansas Inventory of Parental Perceptions Positive Contributions Scale Follow-up: mean 2	The mean parental positive perceptions in the control groups was 0.09 standard deviations higher at post-treatment compared to pre-treatment ¹	The mean parental positive perceptions in the intervention groups was 0.28 standard deviations lower (0.87 lower to 0.32 higher) ³	44 (1 study ⁷)	⊕⊕⊖⊝ low ^{5,6}

years

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

- ¹ This is a difference in standard deviations calculated for the TAU group from change scores before and after the intervention period.
- ² Relative effect for TAU calculated on pre-post change for control groups from Cohen, Howard, and Magiati studies (Remington excluded because only raw scores were reported).
- ³ This is a difference between standard deviations
- ⁴ 4 CCT and 1 RCT
- ⁵ Risk of bias assessment shows mostly equal levels of low risk and high risk. High risk items include allocation concealment, participants and personnel not being blind to treatment status, outcome assessors not being blind to treatment status, and significant differences on key variables at baseline measurement
- ⁶ Small number of included studies precludes our ability to examine funnel plot and thereby cannot exclude the potential of publication bias
- ⁷ Remington 2007

10 Additional tables

10.1 TABLE 1: OUTCOME ASSESSMENTS USED BY STUDY AND MEASUREMENT TIME POINT

		Treatment Groups		Comparison Groups	
Study	Outcomes	Pre-Treatment	Post-Treatment	Pre-Treatment	Post-Treatment
Cohen et al. (2006)	Adaptive behavior	Vineland Adaptive Behavior Scales (VABS; <u>Sparrow 1984</u>)	VABS	VABS	VABS
	IQ	Bayley Scales of Infant Development-II (BSID-II; <u>Bayley 1993</u>), Weschler Preschool and Primary Scale of Intelligence (WPPSI-R; <u>Wechsler 1989</u>),	WPPSI-R, BSID-II	WPPSI-R, BSID	WPPSI-R, BSID-II
	Non-verbal IQ	Merrill-Palmer Scale of Mental Tests (MPS; <u>Stutsman 1948</u>)	MPS	MPS	MPS
	Non-verbal social communication	Not Assessed (NA)	NA	NA	NA
	Expressive	Reynell Developmental Language Scales (RDLS;	RDLS	RDLS	RDLS

	communication	Reynell 1990)			
	Receptive communication	RDLS	RDLS	RDLS	RDLS
	Autism severity	NA	NA	NA	NA
	Play	NA	NA	NA	NA
	Social competence	NA	NA	NA	NA
	Quality of life	NA	Class placement	NA	Class placement
Howard et al. (2005)	Adaptive behavior	VABS; Denver Developmental Screening Test II (<u>Frankenbrug 1992</u>), DP-II, Rockford Infant Developmental Evaluation Scales (RIDES; <u>Project RHISE 1979</u>)	VABS, Denver, DP-II, RIDES	VABS	VABS
	IQ	BSID-II, Developmental Profile-II (DP-II; Alpern 1986), WPPSI-R, Stanford-Binet	WPPSI-R, BSID-II, S-B; DAYC, PEP-R, DAS	WPPSI-R, BSID-II, S-B; DAS	WPPSI-R, BSID-II, S-B; DAS

Intelligence Scale-4 (S-B; Thorndike 1986), Developmental Assessment of Young Children (DAYC; Voress 1998), Psychoeducational Profile- Revised (PEP-R; Schopler 1990), Differential Ability Scales (DAS; Elliot 1990) Non-verbal IQ MPS, S-B MPS, S-B, Leiter International MPS, S-B MPS, S-B, Leiter-R
Developmental Assessment of Young Children (DAYC; Voress 1998), Psychoeducational Profile- Revised (PEP-R; Schopler 1990), Differential Ability Scales (DAS; Elliot 1990)
Young Children (DAYC; Voress 1998), Psychoeducational Profile- Revised (PEP-R; Schopler 1990), Differential Ability Scales (DAS; Elliot 1990)
Voress 1998), Psychoeducational Profile- Revised (PEP-R; Schopler 1990), Differential Ability Scales (DAS; Elliot 1990)
Psychoeducational Profile- Revised (PEP-R; Schopler 1990), Differential Ability Scales (DAS; Elliot 1990)
Revised (PEP-R; Schopler 1990), Differential Ability Scales (DAS; Elliot 1990)
1990), Differential Ability Scales (DAS; Elliot 1990)
Scales (DAS; Elliot 1990)
Non-verbal IQ MPS, S-B MPS, S-B, Leiter International MPS, S-B MPS, S-B, Leiter-R
Performance Scale (Leiter-R; Roid 1997)
Non-verbal social NA NA NA NA NA NA Communication
Expressive RDLS, Rosetti Infant – Toddler RDLS, Rosetti, REEL-R, PLS- RDLS, Rosetti, REEL-R, PLS- RDLS, Rosetti, REEL-R, PLS-
communication Language Scale (Rosetti 3, EVT, Expressive One-Word 3, Infant-Toddler 3, EVT, Expressive One-Word
1990), Receptive Expressive Picture Vocabulary Test Developmental Assessment, Picture Vocabulary Test,
Emergent Language Scales – (Brownell 2000a), Infant- EVT, DP-II Infant-Toddler Developmental
Revised (REEL-R; Bzoch Toddler Developmental Assessment
1991), Preschool Language Assessment
Scale-3 (PLS-3; Zimmerman
1992), Infant-Toddler

	Developmental Assessment (Provence 1985), Expressive Vocabulary Test (EVT; Williams 1997), DP-II			
Receptive communication	RDLS, Rosetti, REEL-R, PLS-3, Infant-Toddler Developmental Assessment-1, Peabody Picture Vocabulary Test (PPVT-III; Dunn 1997a), DP-II	RDLS, Rosetti, REEL-R, PLS-3, PPVT-III, Receptive One-Word Picture Vocabulary Test (Brownell 2000b), Infant-Toddler Developmental Assessment-1	RDLS, Rosetti, REEL-R, PLS- 3, Infant-Toddler Developmental Assessment-1, PPVT-III, DP-II	RDLS, Rosetti, REEL-R, PLS- 3, PPVT-III, Receptive One- Word Picture Vocabulary Test, Infant-Toddler Developmental Assessment-1
Autism severity	# of DSM-IV criteria (APA 1994)		# of DSM-IV criteria	
Play	NA	NA	NA	NA
Social competence	NA	NA	NA	NA
Quality of life	NA	NA	NA	NA

Magiati et al. (2007)	Adaptive behavior	VABS	VABS	VABS	VABS
	IQ	WPPSI-R, BSID-R, MPS	WPPSI-R, BSID-R, MPS	WPPSI-R, BSID-R, MPS	WPPSI-R, BSID-R, MPS
	Non-verbal IQ NA				
	Non-verbal social communication	NA	NA	NA	NA
	Expressive communication	Expressive One-Word Picture Vocabulary Test -Revised (EOWPVT-R; Gardner 1990),	EOWPVT-R	EOWPVT-R	EOWPVT-R
	Receptive communication	British Picture Vocabulary Scale (BPVS-II; Dunn 1997b)	BPVS-II	BPVS-II	BPVS-II
	Autism severity	Autism Diagnostic Interview- Revised (ADI-R; Lord 1994)	ADI-R	ADI-R	ADI-R
	Play	Symbolic Play Test (SPT-II; Lowe 1988)	SPT-II, Test of Pretend Play (Lewis 1997)	SPT-II	SPT-II, Test of Pretend Play
	Social competence	NA	NA	NA	NA

Quality of life NA NA NA NA

Remington et al. (2007)	Adaptive behavior	VABS	VABS	VABS	VABS
	IQ	BSID-R, S-B	BSID-R, S-B	BSID-R, S-B	BSID-R, S-B
	Non-verbal IQ	NA	NA	NA	NA
	Non-verbal social communication	Early Social Communication Scales (ESCS; Mundy 1996)	ESCS	ESCS	ESCS
	Expressive communication	RDLS	RDLS	RDLS	RDLS
	Receptive communication	RDLS	RDLS	RDLS	RDLS
	Autism severity	Autism Screening Questionnaire (ASQ; Berument 1999)	ASQ	ASQ	ASQ
	Play	NA	NA	NA	NA
	Social competence	Positive Social subscale of the Nisonger Child Behavior	Positive Social subscale of the CBRF	Positive Social subscale of the CBRF	Positive Social subscale of the CBRF

	Rating Form (CBRF; Aman 1996)			
Quality of life	Hospital Anxiety and Depression Scale (Zigmond 1983), Parent and Family Problems subscale of the Questionnaire on Resources and Stress-Friedrich-short form (Friedrich 1983), Kansas Inventory of Parent Perceptions Positive Contributions subscale (KIPP; Behr 1992)	Child school placement, Hospital Anxiety and Depression Scale, Parent and Family Problems subscale of the Questionnaire on Resources and Stress- Friedrich-short form, KIPP	Child school placement, Hospital Anxiety and Depression Scale, Parent and Family Problems subscale of the Questionnaire on Resources and Stress- Friedrich-short form, KIPP	Child school placement, Hospital Anxiety and Depression Scale, Parent and Family Problems subscale of the Questionnaire on Resources and Stress- Friedrich-short form, KIPP

Smith et al. (2000)	Adaptive behavior	VABS	VABS	VABS	VABS	
	IQ	BSID-R, S-B	BSID-R, S-B	BSID-R, S-B	BSID-R, S-B	
	Non-verbal IQ	MPS	MPS	MPS	MPS	
	Non-verbal social communication	NA	NA	NA	NA	
	Expressive communication	RDLS	RDLS	RDLS	RDLS	
	Receptive communication	RDLS	RDLS	RDLS	RDLS	
	Autism severity	NA	NA	NA	NA	
	Play	NA	NA	NA	NA	
	Social competence	NA	Child Behavior Checklist (CBCL; Achenbach 1991)	NA	CBCL	
	Achievement	Weschler Individual	WAIT	WAIT	WAIT	

	Achievement Test (WAIT; Weschler 1992), Early Learning Measure (Smith 1995)			
Quality of life	NA	Class placement, Family Satisfaction Questionnaire	NA	Class placement, Family Satisfaction Questionnair

10.2 TABLE 2: OUTCOME ASSESSMENTS USED BY STUDY AND MEASUREMENT TIME POINT

Protocol	Reason not used
Inclusion of random sequence generation and allocation in risk of bias table	Removed from risk of bias due to inclusion of mostly CCTs.
Calculation of mean difference effect size	Across most outcomes SMD needed to be used so we decided to report all ES using SMD.
Reporting of multiple outcome time points	Studies included in review only included one time point, which was immediately after treatment.
Did not have to adjust for missing data	Included studies had few instances of missing data.
Did not have to adjust for unit of analyses issues	No study with multiple treatment groups was located.
Did not combine TAU groups of Howard 2006 study	The autism programming TAU group received intervention that was more similar to the TAU groups from the other included studies, thus it was used and the data from the other group was discarded.
Did not conduct subgroup analyses	Small number of studies.

Did not conduct sensitivity analyses

Small number of studies.

11 Figures

Figure 1: Study flow diagram

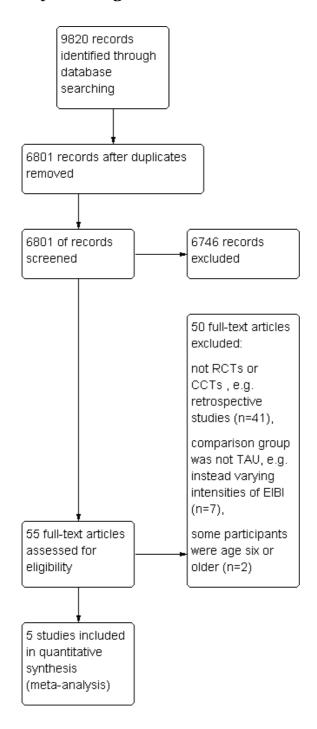


Figure 2: Forest plot of comparison: 1 Adaptive behavior, outcome: 1.1 Vineland Adaptive Behavior Composite

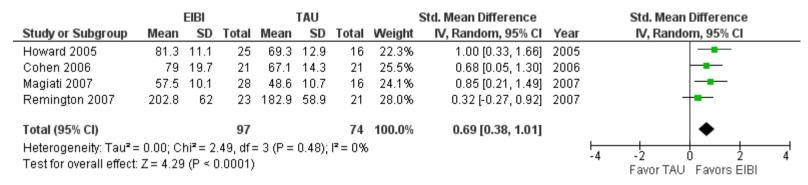


Figure 3: Forest plot of comparison: 3 Intelligence, outcome: 3.1 IQ

		EIBI			TAU		!	Std. Mean Difference		Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year	IV, Random, 95% CI
Howard 2005	89.9	20.9	26	62.1	19.6	16	21.8%	1.34 [0.64, 2.03]	2005	
Cohen 2006	86.8	25	21	73.2	19.5	21	26.0%	0.60 [-0.02, 1.21]	2006	 •
Remington 2007	78.4	17.6	28	65.3	18	16	25.0%	0.73 [0.09, 1.36]	2007	
Magiati 2007	73.5	27.3	23	60.1	27.8	21	27.2%	0.48 [-0.12, 1.08]	2007	-
Total (95% CI)			98			74	100.0%	0.76 [0.40, 1.11]		•
Heterogeneity: Tau² = Test for overall effect:				-	0.28);	I²= 21°	%		<u>⊢</u> -4	4 -2 0 2 4 Favors TAU Favors EIBI

Figure 4: Forest plot of comparison: 4 Communication and language skills, outcome: 4.1 Expressive language

		EIBI			TAU			Std. Mean Difference		Std. M	ean Differ	ence	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year	IV, R	andom, 95	% CI	
Howard 2005	70.5	22.9	26	47.7	23.4	15	31.2%	0.97 [0.30, 1.64]	2005		-	_	
Cohen 2006	52.6	15.6	21	45.7	18.2	20	34.9%	0.40 [-0.22, 1.02]	2006		+		
Magiati 2007	13	17.3	27	10.2	13.7	15	33.9%	0.17 [-0.46, 0.80]	2007		+		
Total (95% CI)			74			50	100.0%	0.50 [0.05, 0.95]			•		
Heterogeneity: Tau² = Test for overall effect	-		-	= 2 (P =	0.22);	I² = 34°	%		⊢ -4	-2 Favors	0 TAU Favo	2 ors EIBI	4

Figure 5: Forest plot of comparison: 4 Communication and language skills, outcome: 4.2 Receptive language

		EIBI			TAU			Std. Mean Difference		Std	. Mean D)ifferei	nce	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year	IV,	Randor	n, 95%	CI	
Howard 2005	71.3	22.7	26	49.9	19.6	15	30.3%	0.97 [0.30, 1.64]	2005			-	-	
Cohen 2006	51	14.8	21	44.6	15.7	20	35.8%	0.41 [-0.21, 1.03]	2006		+	-		
Magiati 2007	20.8	20.8	27	13.2	17.8	15	33.9%	0.38 [-0.26, 1.01]	2007		+	•		
Total (95% CI)			74			50	100.0%	0.57 [0.20, 0.94]				•		
Heterogeneity: Tau² = Test for overall effect:			-	= 2 (P =	0.37);	I ² = 0%	•			-4 -2 Favo	0 rs TAU	Favors	2 EIBI	4

Figure 6: Forest plot of comparison: 4 Communication and language skills, outcome: 4.3 VABS Communication

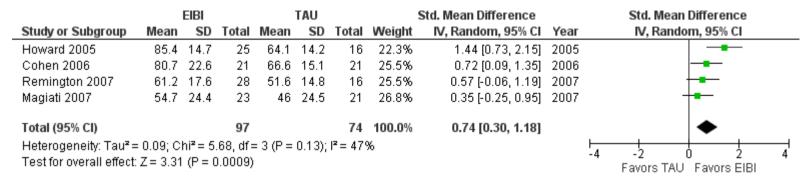
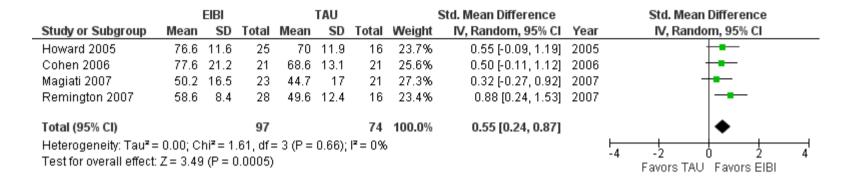


Figure 7: Forest plot of comparison: 5 Social competence, outcome: 5.1 VABS Socialization

		EIBI			TAU			Std. Mean Difference		Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year	IV, Random, 95% CI
Howard 2005	82.1	11.7	25	75	18	16	23.5%	0.48 [-0.16, 1.12]	2005	+-
Cohen 2006	85.5	14.1	21	75.2	18	21	24.7%	0.63 [0.00, 1.25]	2006	 •
Remington 2007	61.8	10.4	28	56.7	10.3	16	24.6%	0.48 [-0.14, 1.11]	2007	 • -
Magiati 2007	43.5	15.9	23	41.5	15.4	21	27.2%	0.13 [-0.47, 0.72]	2007	-
Total (95% CI)			97			74	100.0%	0.42 [0.11, 0.73]		*
Heterogeneity: Tau ² =				= 3 (P =	0.69);	$I^2 = 0\%$)		⊢	4 -2 0 2 4
Test for overall effect:	Z = 2.67	'(P=(0.008)							Favors TAU Favors EIBI

Figure 8: Forest plot of comparison: 6 Quality of life, outcome: 6.1 VABS Daily Living Skills



12 Characteristics of studies

CHARACTERISTICS OF INCLUDED STUDIES [ORDERED BY STUDY ID]

Cohen 2006

Methods	Clinical controlled trial VABS
Participants	21 children with autism in EIBI and 21 children with autism in TAU
Interventions	EIBI included 35- 40 hours per week. TAU included eclectic treatment provided by public schools
Outcomes	Primary outcome: IQ Secondary outcomes: Nonverbal IQ; Language; Adaptive behavior Quality of life measured at post treatment through classroom placement
Notes	Assignment to groups was based on parent preferences. Children had to have IQ greater than 35

Bias	Authors' judgement	Support for judgement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Outcome data missing for 5 of 42 participants (3 EIBI and 2 TAU)
Selective reporting (reporting bias)	Low risk	All collected data appears to be reported

Blinding of participants and personnel (performance bias) All outcomes	High risk	Due to nature of intervention, participants and key personnel likely not blind to treatment status
Blinding of outcome assessment (detection bias) All outcomes	High risk	Parents were not blind to treatment status and were respondents for primary outcome measure; other outcome assessors were blind to treatment status
Protection against contamination	Low risk	There was no evidence reported that the comparison group received EIBI
Baseline measurement	Low risk	No significant differences between groups at baseline

Howard 2005

Methods	Clinical controlled trial
Participants	29 children received EIBI and 16 children received TAU.
Interventions	EIBI consisted of 25-30 hours perweek.TAUwas autismspecific programming provided by public schools
Outcomes	Primary outcome: IQ Secondary outcomes: Nonverbal IQ; Langauge; Adaptive behavior Quality of life not measured
Notes	Assignment to groups was made by the child's IFSP or IEP teams and based heavily on parent preferences

Bias	Authors' judgement	Support for judgement
Incomplete outcome data (attrition bias) All outcomes	High risk	Outcome datamissing for 8 of 37 (22%) participants receiving EIBI and 9 of 41 (22%) participants receiving TAU
Selective reporting (reporting bias)	Low risk	All collected data appears to be reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Due to nature of intervention, participants and key personnel likely not blind to treatment status
Blinding of outcome assessment (detection bias) All outcomes	High risk	Parents were not blind to treatment status and were respondents for primary outcome measure; other outcome assessors were blind to treatment status

Protection against contamination	Low risk	There was no evidence reported that the comparison group received EIBI
Baseline measurement	High risk	EIBI group significantly younger at baseline compared to TAU

Magiati 2007

Methods	Clinical controlled trial
Participants	29 children received EIBI and 16 children received TAU.
Interventions	EIBI consisted of 25-30 hours per week. TAU was autismspecific programming provided by public schools
Outcomes	Primary outcome: IQ Secondary outcomes: Nonverbal IQ; Langauge; Adaptive behavior Quality of life not measured
Notes	Assignment to groups was made by the child's IFSP or IEP teams and based heavily on parent preferences

Bias	Authors' judgement	Support for judgement
Incomplete outcome data (attrition bias) All outcomes	Low risk	0% attrition reported
Selective reporting (reporting bias)	Low risk	All collected data appears to be reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Due to nature of intervention, participants and key personnel likely not blind to treatment status
Blinding of outcome assessment (detection bias) All outcomes	High risk	Parents were not blind to treatment status and were respondents for primary outcome measure; other outcome assessors not blind to treatment status

Protection against contamination	Low risk	There was no evidence reported that the comparison group received EIBI
Baseline measurement	High risk	EIBI group had significantly higher IQ, Vineland Adaptive Behavior Composite, and Vineland Socialization domain at baseline compared to TAU

Remington 2007

Methods	Clinical controlled trial
Participants	23 children who received EIBI and 21 children who received TAU
Interventions	EIBI consisted of more than 25 hours per week. TAU was autism specific programming provided by public schools
Outcomes	Primary outcome: IQ Secondary outcomes: Langauge; Adaptive behavior; Joint Attention; Psychopathology Quality of life through parent well being questionnaires
Notes	Assignment to groups was based on parent preferences

Bias	Authors' judgement	Support for judgement
Incomplete outcome data (attrition bias) All outcomes	Low risk	0% attrition reported
Selective reporting (reporting bias)	Low risk	All collected data appears to be reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Due to nature of intervention, participants and key personnel likely not blind to treatment status
Blinding of outcome assessment (detection bias) All outcomes	High risk	Parents were not blind to treatment status and were respondents for primary outcome measure; other outcome assessors were blind to treatment status

Protection against contamination	Low risk	There was no evidence reported that the comparison group received EIBI
Baseline measurement	High risk	EIBI group significantly younger than TAU group

Smith 2000

Methods	Randomized control trial
Participants	15 children who received EIBI and 13 children who received TAU
Interventions	EIBI consisted of more than 24 hours per week. TAU was parent training
Outcomes	Primary outcome: IQ Secondary outcomes: Nonverbal IQ; Language; Adaptive behavior; Psychopathology Quality of life measured by class placement
Notes	Random assignment to groups. Children had to have IQ greater than 35 and less than 75

Bias	Authors' judgement	Support for judgement
Incomplete outcome data (attrition bias) All outcomes	Low risk	0% attrition reported
Selective reporting (reporting bias)	Low risk	All collected data appears to be reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Due to nature of intervention, participants and key personnel likely not blind to treatment status
Blinding of outcome assessment (detection bias) All outcomes	High risk	Parents were not blind to treatment status and were respondents for primary outcome measure; other outcome assessors were blind to treatment status

Protection against contamination	Low risk	Although the parents of the comparison group were trained n behavioral methods, there was no evidence that the control group received intensive intervention
Baseline measurement	Low risk	No significant differences between groups at baseline

CHARACTERISTICS OF EXCLUDED STUDIES [ORDERED BY STUDY ID]

Study	Reason for exclusion
Eikeseth 2007	Not all participants began treatment before their 6th birthday
Lovaas 1987	Comparison group was less intensive EIBI (not TAU)
Sallows 2005	Comparison group was parent-managed EIBI with similar intensity as clinic-managed EIBI (not TAU)

13 Data and analyses

Comparison 1: Adaptive behavior

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Vineland Adaptive Behavior Composite	4	171	Std. Mean Difference (IV, Random, 95% CI)	0.69 [0.38, 1.01]

Comparison 2: Psychopathology

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Symptom severity	2		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
1.1 Autism Diagnostic Interview-Revised	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.2 Autism Screening Questionnaire	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.3 Developmental Behavior Checklist: Autism Algorithm	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2 Problem behavior	2		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
2.1 Developmental Behavior Checklist: Problem Behavior			Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

2.2 Child Behavior Checklist: 1 Parent	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.3 Child Behavior Checklist: 1 Teacher	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Comparison 3: Intelligence

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
<u>110</u>	4	172	Std. Mean Difference (IV, Random, 95% CI)	0.76 [0.40, 1.11]

Comparison 4: Communication and language skills

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Expressive language	3	124	Std. Mean Difference (IV, Random, 95% CI)	0.50 [0.05, 0.95]
2 Receptive language	3	124	Std. Mean Difference (IV, Random, 95% CI)	0.57 [0.20, 0.94]
3 VABS communication	4	171	Std. Mean Difference (IV, Random, 95% CI)	0.74 [0.30, 1.18]

Comparison 5: Social competence

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 VABS socialization	4	171	Std. Mean Difference (IV, Random, 95% CI)	0.42 [0.11, 0.73]

Comparison 6: Quality of life

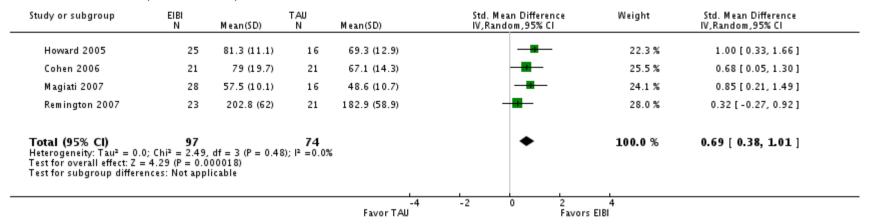
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 VABS Daily Living Skills	4	171	Std. Mean Difference (IV, Random, 95% CI)	0.55 [0.24, 0.87]
2 Academic placement			Other data	No numeric data
3 Parental stress	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected

4 Parental anxiety and depression	1	Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
5 Parental positive perceptions	1	Std. Mean Difference (IV, Random, 95% CI)	Totals not selected

Analysis 1.1: Comparison 1 Adaptive behavior, Outcome 1 Vineland Adaptive Behavior Composite.

Review: Early intensive behavioral intervention (EIBI) for young children with autism spectrum disorders (ASD) Comparison: 1 Adaptive behavior

Outcome: 1 Vineland Adaptive Behavior Composite



Analysis 2.1: Comparison 2 Psychopathology, Outcome 1 Symptom severity

Review: Early intensive behavioral intervention (EIBI) for young children with autism spectrum disorders (ASD) Comparison: 2 Psychopathology Outcome: 1 Symptom severity

Study or subgroup	EIBI N	Mean(SD)	TAU N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Std. Mean Difference IV,Random,95% CI
1 Autism Diagnostic Inte Magiati 2007	rview-Revised 26	30.7 (8.8)	16	34.9 (9.9)		-0.45 [-1.08, 0.18]
2 Autism Screening Ques Remington 2007	tionnaire 23	17.9 (5.9)	16	19.4 (7.3)		-0.23 [-0.87, 0.41]
3 Developmental Behavio Remington 2007	or Checklist: Au 23	tism Algorithm 19.2 (9.5)	16	25.4 (11.4)		-0.59 [-1.24, 0.06]
				-4	-2 0 2	4
				Favors EIBI		ors TAU

Analysis 2.2: Comparison 2 Psychopathology, Outcome 2 Problem behavior

Review: Early intensive behavioral intervention (EIBI) for young children with autism spectrum disorders (ASD) Comparison: 2 Psychopathology Outcome: 2 Problem behavior

Study or subgroup	EIBI N	Mean(SD)	TAU N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Std. Mean Difference IV,Random,95% CI
1 Developmental Behavior	Checklist: Pro	oblem Behavior				
Remington 2007	23	44.9 (22.6)	16	57.9 (22.1)		-0.57 [-1.22, 0.08]
2 Child Behavior Checklist Smith 2000	t: Parent 15	59.2 (9.6)	13	61.4 (9.1)		-0.23 [-0.97, 0.52]
3 Child Behavior Checklist Smith 2000	t: Teacher 15	58.9 (8.8)	13	60 (5.9)		-0.14 [-0.88, 0.60]
					-2 0 2	4
				-4 Favors EIBI	-2 0 2 Favors 1	rau [*]

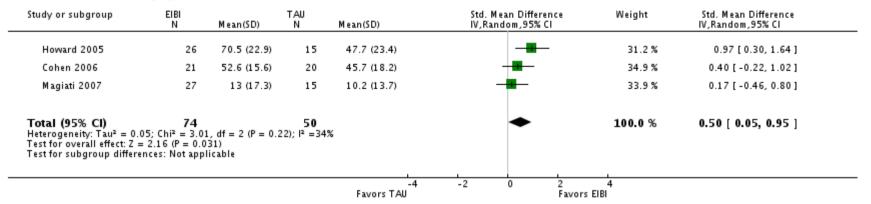
Analysis 3.1: Comparison 3 Intelligence, Outcome 1 IQ

Review: Early intensive behavioral intervention (EIBI) for young children with autism spectrum disorders (ASD) Comparison: 3 Intelligence Outcome: 1 IQ

Study or subgroup	EIBI N	Mean(SD)	TAU N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Howard 2005	26	89.9 (20.9)	16	62.1 (19.6)	-	21.8 %	1.34 [0.64, 2.03]
Cohen 2006	21	86.8 (25)	21	73.2 (19.5)	-	26.0 %	0.60 [-0.02, 1.21]
Remington 2007	28	78.4 (17.6)	16	65.3 (18)	-	25.0 %	0.73 [0.09, 1.36]
Magiati 2007	23	73.5 (27.3)	21	60.1 (27.8)	-	27.2 %	0.48 [-0.12, 1.08]
Total (95% CI) Heterogeneity: Tau² = 0. Test for overall effect: Z = Test for subgroup differe	=4.16 (P = 0.0)	00032)	74 28); I² =219	6	•	100.0 %	0.76 [0.40, 1.11]
				-4 Favors TAU	-2 0 2 Favors	4 EIBI	

Analysis 4.1: Comparison 4 Communication and language skills, Outcome 1 Expressive language

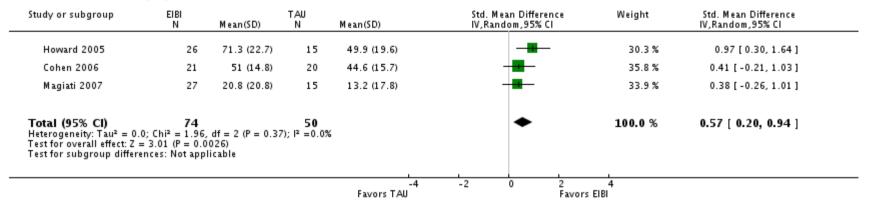
Review: Early intensive behavioral intervention (EIBI) for young children with autism spectrum disorders (ASD) Comparison: 4 Communication and language skills Outcome: 1 Expressive language



Analysis 4.2: Comparison 4 Communication and language skills, Outcome 2 Receptive language

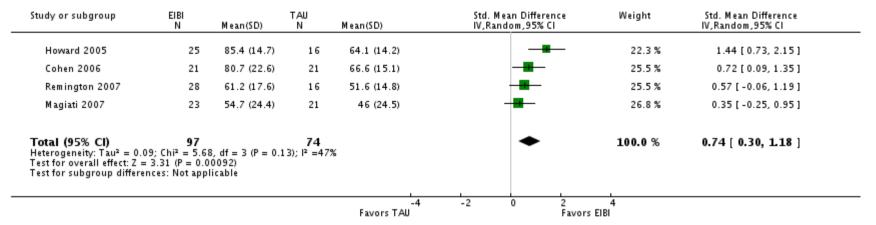
Review: Early intensive behavioral intervention (EIBI) for young children with autism spectrum disorders (ASD) Comparison: 4 Communication and language skills

Outcome: 2 Receptive language



Analysis 4.3: Comparison 4 Communication and language skills, Outcome 3 VABS communication

Review: Early intensive behavioral intervention (EIBI) for young children with autism spectrum disorders (ASD) Comparison: 4 Communication and language skills Outcome: 3 VABS communication



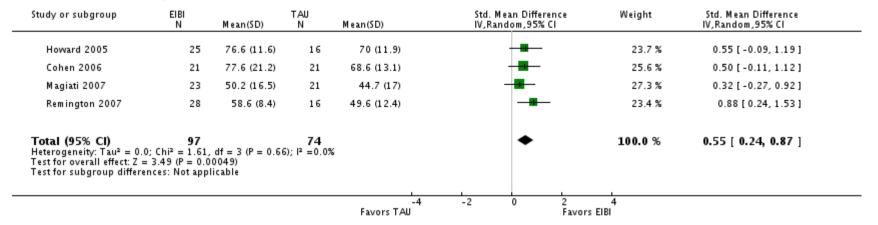
Analysis 5.1: Comparison 5 Social competence, Outcome 1 VABS socialization

Review: Early intensive behavioral intervention (EIBI) for young children with autism spectrum disorders (ASD) Comparison: 5 Social competence Outcome: 1 VABS socialization

Study or subgroup	EIBI N	Mean(SD)	TAU N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
		Mean(SD)	.,	Mean(3D)	IV, Kalidolii, 55% Ci		IV, Kalidolli, 55% Cl
Howard 2005	25	82.1 (11.7)	16	75 (18)	 -	23.5 %	0.48 [-0.16, 1.12]
Cohen 2006	21	85.5 (14.1)	21	75.2 (18)	-	24.7 %	0.63 [0.00, 1.25]
Remington 2007	28	61.8 (10.4)	16	56.7 (10.3)	-	24.6 %	0.48 [-0.14, 1.11]
Magiati 2007	23	43.5 (15.9)	21	41.5 (15.4)	-	27.2 %	0.13 [-0.47, 0.72]
Total (95% CI) Heterogeneity: Tau² = 0.0 Test for overall effect: Z =			74 9); l² =0.0%	;	•	100.0 %	0.42 [0.11, 0.73]
Test for subgroup differe	nces: Not app	licable					
				-4 Favors TAU	-2 0 2 Favors	4 : FIBI	

Analysis 6.1: Comparison 6 Quality of life, Outcome 1 VABS Daily Living Skills

Review: Early intensive behavioral intervention (EIBI) for young children with autism spectrum disorders (ASD) Comparison: 6 Quality of life Outcome: 1 VABS Daily Living Skills



Analysis 6.2: Comparison 6 Quality of life, Outcome 2 Academic placement

Academic placement

Study	EIBI N		EIBI general ed- ucation with sup- port		TAU general education with no extra support	
Cohen 2006	21	6	10	21	0	1
Smith 2000	15	4	2	130	0	1

Analysis 6.3: Comparison 6 Quality of life, Outcome 3 Parental stress.

Review: Early intensive behavioral intervention (EIBI) for young children with autism spectrum disorders (ASD) Comparison: 6 Quality of life Outcome: 3 Parental stress

EIBI N	Mean(SD)	TAU N	Mean(SD)						Std. Mean Difference IV,Random,95% CI	
23	8.73 (3.3)	21	7.95 (2.45)			•			0.26 [-0.33, 0.86]	
				-100	-50	0	50	100		
	N	N Mean(SD)	N Mean(SD) N 23 8.73 (3.3) 21	N Mean(SD) N Mean(SD) 23 8.73 (3.3) 21 7.95 (2.45)	N Mean(SD) N Mean(SD) 23 8.73 (3.3) 21 7.95 (2.45) -100	N Mean(SD) N Mean(SD) IV,Ran 23 8.73 (3.3) 21 7.95 (2.45) -100 -50	N Mean(SD) N Mean(SD) IV,Random,95	N Mean(SD) N Mean(SD) IV,Random,95% CI 23 8.73 (3.3) 21 7.95 (2.45) -100 -50 0 50	N Mean(SD) N Mean(SD) IV,Random,95% CI 23 8.73 (3.3) 21 7.95 (2.45) -100 -50 0 50 100	N Mean(SD) N Mean(SD) IV,Random,95% CI IV,Random,95% CI 23 8.73 (3.3) 21 7.95 (2.45) 0.26 [-0.33, 0.86]

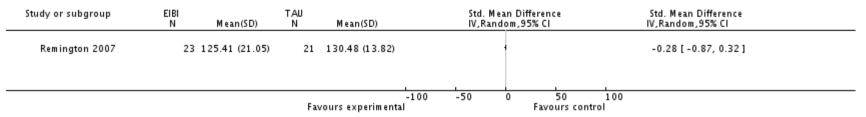
Analysis 6.4: Comparison 6 Quality of life, Outcome 4 Parental anxiety and depression

Review: Early intensive behavioral intervention (EIBI) for young children with autism spectrum disorders (ASD) Comparison: 6 Quality of life Outcome: 4 Parental anxiety and depression

Study or subgroup	EIBI N	Mean(SD)	T AU N	Mean(SD)		Std. Mo IV,Ran		fference 15% Cl		Std. Mean Difference IV,Random,95% CI	
Remington 2007	23	7.9 (4.73)	21	7.4 (4.08)						0.11 [-0.48, 0.70]	
					-100	-50	ᢐ	50	100		
			Fav	ours experimenta	I			Favours co	ntrol		

Analysis 6.5: Comparison 6 Quality of life, Outcome 5 Parental positive perceptions

Review: Early intensive behavioral intervention (EIBI) for young children with autism spectrum disorders (ASD) Comparison: 6 Quality of life Outcome: 5 Parental positive perceptions



14 Appendices

APPENDIX 1. SEARCH STRATEGIES

Cochrane Central Register of Controlled Trials (CENTRAL), part of The Cochrane Library

```
#1MeSH descriptor Early Intervention (Education), this term only
#2MeSH descriptor Behavior Therapy, this term only
#3Lovaas*
#4(intens* NEAR/3 (intervent* or therap* or treat* or program*))
#5(IBI or EIBI)
#6applied NEXT behavio* NEXT analy* or ABA
#7(#1 OR #2 OR #3 OR #4 OR #5 OR #6)
#8MeSH descriptor Child Development Disorders, Pervasive explode all trees
#9(pervasive development* disorder* or PDD or PDDs)
#10Rett*
#11Asperger*
#12autis* or ASD or ASDs
#13Kanner*
#14childhood schizophren*
#15MeSH descriptor Communication Disorders, this term only
#16MeSH descriptor Speech Disorders, this term only
#17MeSH descriptor Language Development Disorders, this term only
#18MeSH descriptor Child Behavior Disorders, this term only
#19communicat* NEAR/3 disorder*
#20speech NEAR/3 (delay* or disorder*)
#21(child* NEAR/3 behavio* NEAR/3 disorder*)
#22(language NEAR/3 (delay* or disorder*))
#23(#8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR
#18 OR #19 OR #20 OR #21 OR #22)
#24(baby or babies or infant* or toddler* or child* or pre-school* or preschool* or
boy* or girl*)
#25MeSH descriptor Child explode all trees
#26MeSH descriptor Infant, this term only
#27(#24 OR #25 OR #26)
#28(#7 AND #23 AND #27)
```

Ovid MEDLINE(R)

- 1 "Early Intervention (Education)"/ (1408)
- 2 behavior therapy/ (21938)
- 3 Lovaas\$.tw. (32)
- 4 (intens\$ adj3 (interven\$ or therap\$ or treat\$ or program\$)).tw. (32188)
- 5 (IBI or EIBI).tw. (316)
- 6 (applied behavio\$ analy\$ or ABA).tw. (4419)
- 7 or/1-6 (59640)
- 8 exp Child Development Disorders, Pervasive/ (16396)
- 9 (pervasive development\$ disorder\$ or PDD or PDDs).tw. (2681)
- 10 (autis\$ or ASD or ASDs).tw. (19180)
- 11 Asperger\$.tw. (1310)
- 12 Kanner\$.tw. (163)
- 13 Rett\$.tw. (2547)
- 14 childhood schizophrenia.tw. (240)
- 15 communication disorders/ (1333)
- 16 (communicat\$ adj3 disorder\$).tw. (1510)
- 17 Speech Disorders/ (9473)
- 18 language development disorders/ (4129)
- 19 (speech adj3 (delay\$ or disorder\$)).tw. (3207)
- 20 (language adj3 (delay\$ or disorder\$)).tw. (3213)
- 21 child behavior disorders/ (17384)
- 22 (child\$ adj3 behavio\$ adj3 disorder\$).tw. (963)
- 23 or/8-22 (59556)
- 24 infant/ (589750)
- 25 exp child/ (1430402)
- 26 (baby or babies or infant\$ or toddler\$ or child\$ or pre-school\$ or preschool\$ or boy\$ or girl\$).tw. (1140302)
- 27 or/24-26 (1959532)
- 28 7 and 23 and 27 (2254)

Embase (OVID)

- 1 early childhood intervention/ (1092)
- 2 behavior therapy/ (33593)
- 3 Lovaas\$.tw. (34)
- 4 (intens\$ adj3 (interven\$ or therap\$ or treat\$ or program\$)).tw. (40854)
- 5 (IBI or EIBI).tw. (422)
- 6 (applied behavio\$ analy\$ or ABA).tw. (4781)
- 7 or/1-6 (79926)
- 8 exp autism/ (26390)
- 9 (pervasive development\$ disorder\$ or PDD or PDDs).tw. (3574)
- 10 Rett\$.tw. (3077)

- 11 Asperger\$.tw. (1708)
- 12 (autis\$ or ASD or ASDs).tw. (24292)
- 13 Kanner\$.tw. (185)
- 14 childhood schizophrenia.tw. (233)
- 15 (communicat\$ adj3 disorder\$).tw. (1870)
- 16 speech disorder/ (16274)
- 17 communication disorder/ (5448)
- 18 (speech adj3 (delay\$ or disorder\$)).tw. (3988)
- 19 language disability/ (10370)
- 20 (language adj3 (delay\$ or disorder\$)).tw. (3975)
- 21 child behavior disorders/ (36527)
- 22 (child\$ adj3 behavio\$ adj3 disorder\$).tw. (1147)
- 23 or/8-22 (99851)
- 24 7 and 23 (3397)
- 25 (baby or babies or infant\$ or toddler\$ or child\$ or pre-school\$ or preschool\$ or

boy\$ or girl\$).tw. (1294111)

- 26 exp child/ (1502446)
- 27 25 or 26 (1973130)
- 28 24 and 27 (2290)

PsycINFO (OVID)

- 1 early intervention/ (7513)
- 2 behavior therapy/ (11741)
- 3 behavior modification/ (9732)
- 4 Lovaas.tw. (112)
- 5 (intens\$ adj3 (interven\$ or therap\$ or treat\$ or program\$)).tw. (6775)
- 6 (IBI or EIBI).tw. (169)
- 7 (applied behavio\$ analy\$ or ABA).tw. (1645)
- 8 or/1-7 (36141)
- 9 exp pervasive developmental disorders/ (20289)
- 10 (pervasive development\$ disorder\$ or PDD or PDDs).tw. (2660)
- 11 Rett\$.tw. (794)
- 12 Asperger \$.tw. (2452)
- 13 (autis\$ or ASD or ASDs).tw. (23971)
- 14 Kanner\$.tw. (356)
- 15 childhood schizophrenia.tw. (488)
- 16 communication disorders/ (1553)
- 17 (communicat\$ adj3 disorder\$).tw. (1880)
- 18 (speech adj3 (delay\$ or disorder\$)).tw. (4152)
- 19 (language adj3 (delay\$ or disorder\$)).tw. (5021)
- 20 language disorders/ or language delay/ (6130)
- 21 speech disorders/ or retarded speech development/ (3864)
- 22 behavior disorders/ (7442)

23 or/9-22 (48448)

24 ("140" or "160" or "180").ag. (257053)

25 (baby or babies or infant\$ or toddler\$ or child\$ or pre-school\$ or preschool\$ or boy\$ or girl\$).tw. (549496)

26 24 or 25 (610720)

27 8 and 23 and 26 (2440)

CINAHL Plus (EBSCOhost)

S24 S7 and S20 and S23

S23 S21 or S22

S22 BABY OR BABIES OR INFANT* OR toddler* or child* or pre-school* or preschool* or boy* or girl*

S21 AG infant or AG CHILD OR AG CHILD, PRESCHOOL

S20 S8 or S9 or S10 or S11 or S12 or S13 or S14 or S15 or S16 or S17 or S18 or S19

S19 (MH "Child Behavior Disorders")

S18 language N3 delay or language N3 disorder*

S17 speech N3 delay* or speech N3 disorder*

S16 COMMUNICAT* N3 DISORDER*

S15 (MH "Communicative Disorders") OR (MH "Language Disorders") OR (MH "Speech Disorders")

S14 childhood schizophren*

S13 Kanner*

S12 (autis* or ASD or ASDs)

S11 Asperger*

S10 Rett*

S9 (pervasive development* disorder* or PDD or PDDs)

S8 (MH "Child Development Disorders, Pervasive+")

S7 S1 or S2 or S3 or S4 or S5 or S6

S6 (applied behavio* analy*) or (ABA)

S5 (IBI or EIBI)

S4 (intens* N3 interven*) or (intens* N3 therap*) or (intens* N3 treat*) or (intens*

N3 program*)

S3 lovaas*

S2 (MH "Behavior Therapy") or (MH "Behavior Modification")

S1 (MH "Early Intervention") OR (MH "Early Childhood Intervention")

ERIC Dialog Datastar

"((EARLY-INTERVENTION.DE.) OR (BEHAVIOR-MODIFICATION.DE.) OR ((INTERSIVE NEAR (INTERVENTION\$1 OR THERAP\$3 OR TREATMENT\$1 OR PROGRAM\$3)).TI,AB.) OR ((IBI OR EIBI).TI,AB.)

OR ((APPLIED ADJ BEHAVIOR\$2 ADJ ANALY\$4 OR ABA) .TI,AB.) OR (LOVAAS.TI,AB.)) AND ((AUTISM.W..DE. OR PERVASIVE-DEVELOPMENTAL-

((AUTIS\$3 OR ASPERGER\$1 OR KANNER\$1 OR RETT\$1 OR ASD OR ASDS OR PDD OR PDDS).TI,AB.) OR ((CHILDHOOD ADJ SCHIZOPHRENI\$2).TI,AB.)) AND ((YOUNG-CHILDREN.DE. OR

PRESCHOOL-CHILDREN.DE. OR TODDLERS.W..DE.) OR ((CHILD\$3 OR INFAN\$1 OR TODDLER\$1 OR PRESCHOOL\$3 OR PRE ADJ SCHOOL\$3).TI,AB.))"

SSCI and CPCI-SSH (Web of Science)

#7 AND #6

DocType=All document types; Language=All languages;

#7 TS=(baby or babies or infant* or toddler* or child* or pre-school* or preschool* or boy* or girl*)

DocType=All document types; Language=All languages;

#6 #5 AND #4

DocType=All document types; Language=All languages;

#5 TS=(autis* or asperger* or ASD or ASDs or Pervasive development* disorder* or PDD or PDDs or REtt* or Kanner* or childhood schizophren*)

DocType=All document types; Language=All languages;

#4 #3 OR #2 OR #1

DocType=All document types; Language=All languages;

#3 TS=("applied behav* analy*" or ABA)

DocType=All document types; Language=All languages;

#2 TS=(lovaas OR IBI or EIBI)

DocType=All document types; Language=All languages;

#1 TS=(intens* NEAR/3 (interven* or therap* or treat* or program*))

DocType=All document types; Language=All languages;

Sociological Abstracts (Proquest)

(SU.EXACT("Behavior Modification") OR TI("EIBI" OR "ABA" OR "IBI" OR Lovaas) OR AB("EIBI" OR "ABA" OR "IBI" OR lovaas) OR TI("applied behav* analysis") OR AB("applied behav* analysis") OR TI((intensive) NEAR/3 (interven* OR therapy* OR treat* OR program*))) AND (TI(child* OR baby OR babies OR toddler* OR preschool* OR preschool*) OR AB(child* OR baby OR babies OR toddler* OR preschool* OR preschool*) OR SU.EXACT("Children" OR "Infants")) AND (SU.EXACT("Behavior Modification") OR TI("EIBI" OR "ABA" OR Lovaas) OR AB("EIBI" OR "ABA" OR lovaas) OR TI("applied behav* analysis") OR AB("applied behav* analysis") OR TI((intensive) NEAR/3 (interven* OR therapy* OR treat* OR program*))) AND (SU.EXACT(("Autism")) OR TI(autis* OR asperg* OR "PDD" OR "PDDs" OR "ASD" OR "ASDs" OR kanner* OR childhood schizophren* OR pervasive development* disorder*) OR AB(autis* OR asperg* OR "PDD" OR "PDDs" OR

"ASD" OR "ASDs" OR kanner* OR childhood schizophren* OR pervasive development* disorder*) OR TI((communicat* OR behav*) NEAR/3 disorder*) OR AB((communicat* OR behav*) NEAR/3 disorder*) OR TI ((speech OR language) NEAR/3 (delay* OR disorder*)) OR AB((speech OR language) NEAR/3 (delay* OR disorder*)))

WorldCat (www.worldcat.org)

'kw:("intens* behav*" OR EIBI OR IBI OR ABA OR "applied behav*") AND kw:(autis* OR asd* OR asperg* OR PDD* OR "pervasive development* disorder*")) AND kw:(child* OR infant* OR baby OR babies OR toddler* OR preschool* OR preschool*)' > 'Thesis/dissertation'

mRCT (http://www.controlled-trials.com/mrct/)

2 separate searches were run:

(intens* behav* OR EIBI OR IBI) AND (autis* OR asperg* OR PDD OR ASD OR rett*)

(applied behav* OR ABA) AND (autis* OR asperg* OR PDD OR ASD OR rett*)

NDLTD (http://www.ndltd.org/)

2 separate searches were run:

EIBI IBI "intens* behav*" "applied behav*" in the ABSTRACT Show results in Psychology or Social and Behavioral Sciences

autis* asperg* "pervasive development*" "PDD*" "ASD*" in the ABSTRACT Show results in Psychology or Social and Behavioral Sciences